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SUMMARY OF RECENT ABSTRACTS*

VIII. TYPHUS GROUP OF FEVERS

General

WEYER *et al.* (p. 1075) have examined rickettsiae by the electron microscope, and think that they resemble bacteria rather than viruses in structure and also in composition and behaviour. On the other hand, as a result of study of the action of enzymes on rickettsiae, CALLOT and VENDRELY (p. 990) conclude that rickettsiae are intermediate in structure between bacteria and viruses.

CAMAIN (p. 322) considers that the use of Machiavello's method, and hot Giemsa, is not a sure method of detecting rickettsiae.

Proteus OX19 type: Vectors, louse and flea

Louse typhus

Epidemiology.—MACCARTHY (p. 696) notes the high louse-infestation rates found in people wishing to emigrate from Eire, and examined before doing so, and refers to two outbreaks of typhus in which infection was probably acquired by inhaling infected dust in which rickettsiae had remained virulent for 41 and 15 years respectively.

MORGAN *et al.* (p. 887) report two cases of Brill's disease, the form of louse-borne typhus which occurs as a recrudescence of a latent infection persisting indefinitely after an attack of that form of typhus. The patients migrated from Ireland to the United States 30 or more years ago.

In prisoners and others who returned to France in 1945, 167 cases of typhus were seen in Paris. BOYER (p. 57) shows that there were only 15 cases secondary to these. Doctors and others in contact with repatriated persons were vaccinated with the Durand and Giroud vaccine. In spite of the influx of refugees during the war, and of the epidemic in Spain in 1941–42, there were relatively few cases in Portugal (DIAS, p. 58). It was, however, proved that gypsies introduced it into the country from Spain.

Typhus in a hospital in Finland is described by HIRVONEN (p. 776).

In the town of Jos, Northern Nigeria, louse infestation is heavy, and there was an outbreak of typhus in 1945. MONTGOMERY and BUDDEN (p. 322) soon controlled the epidemic by dusting with DDT. Laboratory examinations made in connexion with this outbreak are reported by FINDLAY and ELMES (p. 322), who isolated rickettsiae from patients and from lice. In a minority of tests

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1948, v. 45. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

some strains reacted more like murine than epidemic rickettsiae, and the authors make the point that both these forms are known in West Africa, and that the tick-borne form also probably occurs there. In the third paper of the series (p. 324) Montgomery describes the clinical features observed, which, he thinks, were unlike those of classical typhus [but in comment MEGAW demurs at this conclusion].

JADIN (p. 325) has isolated orchitic strains of rickettsiae in two cases of the "red fever of the Congo" at Costermansville. In each case the Weil-Felix reaction with *Proteus OX19* was positive, but in two other cases this test was negative or positive at low titre only. JADIN and D'HOOGHE (p. 508), however, claim to have isolated epidemic-typhus rickettsiae from other patients in whom the diagnosis of "red fever" had been made. MEGAW comments that there is now no valid reason for retaining the name.

The epidemiological conditions at Lanchow in North-West China suggested that typhus is louse-borne, and this was corroborated by detailed examination of certain strains isolated (WANG *et al.* p. 777).

Positive results to the Weil-Felix reaction were found (to a titre of 1 in 100) by FLOCH and CAMAIN (p. 250) in a small proportion of sera submitted in French Guiana for the Widal test. They describe a case of murine typhus in man.

A complement fixation test in which *R. prowazeki* was used as antigen indicated that a quarter of the people in a group of villages in Colombia had been infected with typhus, but MONTOYA *et al.* (p. 419) point out that the antigen did not differentiate between the louse-borne and the flea-borne types, though epidemiological conditions suggested the former.

Aetiology, transmission.—RABINOWITZ (p. 986) has cultivated *R. prowazeki* in embryonated eggs killed by chilling on the third day of development.

CLARKE and FOX (p. 986) show that suspensions of *R. mooseri* and *R. prowazeki* cause haemolysis of red cells from rabbits and sheep, but not from certain other animals. The degree of haemolytic activity (which is inhibited by homologous anti-serum) may provide an index of infectivity, and the haemolytic factor may be identical with the rickettsial toxin.

By experiments on chick embryos infected with typhus rickettsiae, and by using *p*-aminobenzoic acid and potassium cyanide, GREIFF and PINKERTON (p. 509) have shown that rickettsial growth is inversely proportional to the respiratory rate of the host cells.

Desiccation of *R. prowazeki* in suspensions from the lungs of mice over calcium chloride *in vacuo* at 15°C. appears to reduce the number of virulent rickettsiae compared with desiccation by the lyophile method at −16°C., when tested by the intradermal route, but GIROUD and VARGUES (p. 1075) found little difference on intraperitoneal injection.

ANIGSTEIN *et al.* (p. 699) infiltrated the skin of guineapigs with anti-organ sera (prepared by inoculating rabbits with spleen or bone-marrow of guinea-pigs), and into the same area, 2 hours later, they injected material infective for typhus. Infection rarely occurred, but the authors do not claim that this procedure can be applied usefully in relation to human disease.

DELBOVE and REYNES (p. 61) have investigated the course of typhus in guineapigs infected with tuberculosis.

KUBICZ (p. 420) cultivates lice in sterile conditions so that they can later be fed on patients suspected of typhus, and the diagnosis can be made by examination of their faeces.

Pathology.—COTRUFO and ZITO (p. 591) have studied the histopathology of the small blood vessels in typhus, and GUERRISI (p. 591) that of the kidneys in the glomerulonephritis sometimes observed in typhus. HORTOPANU (p. 167) discusses the forms of gangrene found in typhus, and their pathology.

DE ROSNAY (p. 166) states that the bone marrow in typhus shows an intense reticulo-endothelial response in the early stages, which may have diagnostic value. REVOL *et al.* (p. 590) have also studied the bone marrow in typhus. A study of the red cell sedimentation rate in typhus has been made by GOYTIA (p. 324).

FRANK and MAY (p. 988) investigated the protective power of human convalescent serum when mixed with rickettsiae of murine or classical typhus before inoculation into animals; the results were very variable. SIEGERT (p. 988) refers to the antitoxic power of serum after typhus, in protecting mice from death after injection of rickettsial toxins. This power is much greater in persons recovered from the disease than in those who have been vaccinated.

Tests.—With carefully prepared antigens of epidemic and murine typhus, PLOTZ *et al.* (p. 699) were able to show that the rickettsia-agglutination test in typhus was positive earlier than the complement-fixation test, and that by both tests it was possible to differentiate between epidemic and murine infections. The agglutination test gave more cross reactions than the complement-fixation test. Similar work on murine typhus was carried out by almost the same team, SCOVILLE *et al.* (p. 700), with similar results. The murine rickettsia-agglutination test was always positive after the 9th day, but the murine complement-fixation test with washed antigen was negative at 10–19 days in most cases, though with non-specific soluble antigens it became positive earlier.

JADIN and GIROUD (p. 592) note that in an epidemic of typhus in Urundi, 18 of 23 sera agglutinated epidemic-typhus rickettsiae at much higher titres than murine rickettsiae. These authors (p. 697) prefer the rickettsia-agglutination test to the complement-fixation test, and make the point that it clearly differentiates between epidemic and murine typhus during the 3rd and 4th days of the attack, and after the height of the attack, but less clearly in the intermediate stage or when the serum has been inactivated by heat or has long been stored.

GIROUD and LE GAC (p. 1076) have done rickettsia-agglutination tests (with murine and epidemic rickettsiae) and Weil-Felix tests, on patients with boutonneuse fever, and conclude that there is an antigen common to epidemic typhus and boutonneuse fever.

SANDOR *et al.* (pp. 166, 986) have studied the relationship of anti-typhus agglutinins in infected animals, to the various euglobulin fractions of serum.

GIROUD *et al.* (p. 60) show that crushed and washed typhus tissues retain appreciable amounts of antigen; and that potent antigens in suspensions of infected animal lungs provoke a rise in rickettsia-agglutinin titre on injection into rabbits. GIROUD and CIACCIO (p. 885) show that soluble antigens from the lungs of rabbits infected with *R. prowazeki* extracted with alcohol are rather more satisfactory than those extracted with saline solution or water.

BERGE (p. 778) has used soluble antigens of *R. prowazeki* and *R. mooseri*, released by extraction with ether, for the complement fixation test. These antigens do not differentiate between the two types of typhus, but the test has a value for screening, and therefore for reducing the need for subsequent more refined tests, in diagnostic and survey work.

The addition of traces of egg yolk to suspensions of yolk sacs infected with various rickettsiae before treatment with ether gives antigens with enhanced complement-fixation titres (HOTTLE and SHEPARD, p. 248).

VAN DER SCHEER *et al.* (p. 60) show that although non-specific reactions with Wassermann-positive sera are given in complement-fixation tests in which yolk-sac rickettsial vaccines extracted with ether are used as antigens, they rarely occur if the vaccines are purified by shaking with benzene and concentrated by precipitation with sodium sulphate. By these tests Rocky

Mountain spotted fever can be distinguished from epidemic and murine typhus, but differentiation of the two last was not easy.

BADENSKI and DROUHET (p. 591) prefer fresh serum to serum inactivated by heat, in the complement-fixation test for typhus.

GIROUD and JUDE (p. 167) quote evidence which indicates that there are specific differences between the agglutinins for *Proteus* and rickettsiae. GAASE (p. 987) shows that agglutinins against *Proteus OX19* are very variable in their resistance to heating at 56°C. for one hour. Thermostability is not valid in differentiating agglutinins derived from infections with *Proteus* from those arising as a result of typhus. HIRSZFELD (p. 697) has isolated strains of *Proteus X* from blood, urine or post-mortem material of patients with typhus.

Clinical findings.—SCHMIEDER (p. 887) has studied the encephalogram in patients showing after-effects of typhus. It has some diagnostic value.

BERCEANU and CUCIUREANU (p. 698) noted that nervous symptoms dominated the clinical picture in 141 of 230 cases of typhus in Bucharest, and that in all 230 there was some degree of cellular reaction in the cerebrospinal fluid. LEMKE (p. 62) gives details of some of the late effects of typhus, especially in relation to the nervous system and the heart.

HORTOPANU (p. 698) relates the comparatively low mortality in typhus of recent years to the improvement which has taken place in the standard of life in European countries, and he comments on the relatively high mortality in people over 40. D'IGNAZIO (p. 888) refers to the recent dramatic fall in the case-fatality rate of typhus in Ethiopia. This is probably the result of improvement in hygienic conditions, louse control and the use of vaccines.

Treatment.—Chloromycetin is described by EHRLICH *et al.* (p. 779), and its great value in prevention and treatment of rickettsial infections of chick embryos and mice is reported by SMADEL and JACKSON (p. 779). In human typhus its remarkable value was shown on a small scale in Colombia by PAYNE *et al.* (p. 779), who gave it by mouth or intravenously. There were no toxic effects. LEY, SMADEL and CROCKER (p. 1076) administered chloromycetin by mouth to normal persons, in various doses, and noted the blood levels. Excretion is rapid and no ill effects were experienced. SMADEL, LÉON, LEY and VARELA (p. 1077) used it in several cases of typhus in Mexico, with good effect. They suggest an initial dose of 40 mgm. per kilo body weight, followed by a daily dose of 35 mgm. per kilo in divided doses at intervals of 2 hours, until improvement occurs ; then a daily dose of 20 mgm. per kilo (divided, every 4 hours) until the 14th day after onset.

GIROUD (p. 420) has shown that streptomycin has a definite effect on typhus rickettsiae when tested intradermally, but much less when mice infected intranasally are treated with it. Certain acridine compounds were found by SMADEL *et al.* (p. 168) to have rickettsiostatic effects in infected chick embryos, but the margin of safety was low. Later (p. 321) the authors showed that streptomycin inhibits the rickettsiae of typhus and Rocky Mountain fever, but not of tsutsugamushi disease, in the same conditions, and that nitroacridine and *p*-aminobenzoic acid have some synergic action with streptomycin.

RENNER (p. 778) has treated a large number of cases of typhus. He distrusts many of the drugs which have been advocated by others, but he has had success by administering cardiovascular tonics, and sedative drugs, only when there are definite indications for them. Convalescent blood is useful [but the author gives little relevant information] only when given up to the third day of illness.

Trials of 17 methods of treatment of typhus were made during 8 years by FERRO-LUZZI and FERRO-LUZZI (p. 249) in Eritrea ; these did not include the use of a *p*-aminobenzoic acid. The only one which seemed to give good results was the administration of aspirin, but in comment MEGAW suggests that the

controls used do not satisfy the requirements necessary for unequivocal acceptance of the value of this treatment.

Vaccination.—BIELING and OELRICHS (p. 886) use the intradermal injection of minute quantities of yolk-sac growth of typhus rickettsiae, as a means of measuring the antigenic potency of the strains. With large doses (and also with killed suspensions) this method provides an appreciable degree of immunity against homologous strains within 7 days. The potency of vaccines can be measured by the quantity of immune serum needed to prevent the Giroud reaction.

In 60 laboratory workers constantly exposed to typhus infection, and protected by the Durand-Giroud vaccine, 12 suffered from mild attacks and 4 from inapparent attacks, all diagnosed by Giroud's intradermal test and rickettsia-agglutination tests (CHEVÉ *et al.*, p. 249).

RUIZ CASTAÑEDA (p. 592) has elaborated a method for purifying and concentrating suspensions of epidemic- and murine-typhus rickettsiae for the preparation of vaccine. He prefers the vaccine containing both types, partly because the murine form may be transmitted from man to man by lice, in epidemic fashion, and he advises that a course of 5 doses should be given, at weekly intervals. ORTIZ MARIOTTE (p. 1077) reports a test of the Castañeda bivalent vaccine in Mexico in 1942–43. There was apparently some benefit, but the numbers are small. Later an improved vaccine gave better results.

FRANKE (p. 777) observed the Weil-Felix titre after inoculation with 3 doses of various vaccines ; the titre rose moderately in most cases, but soon declined.

Control.—By using 10 per cent. DDT in talc or pyrophyllite for body lice, and 5 per cent. phenyl cellosolve for head lice, on several occasions, MONTOYA and OSEJO (p. 989) reduced the infestation rates in a Mexican village to less than 5 per cent. for several months. In another village, and with only one application, the rates were much reduced, but increased again after some months.

Flea typhus

DUNN (p. 781) reports a case, apparently of murine typhus, in a London dock worker much exposed to fleas while unloading cargoes from abroad.

SAVOOR *et al.* (p. 888) have investigated cases of typhus in Bombay City, and conclude that the clinical and epidemiological features are consistent with the diagnosis of flea-borne typhus. They describe a modification of the rapid slide test with *Proteus OX19*. They (p. 1077) have isolated and studied strains identified as *R. mooseri* in Bombay. They report their study of the characteristics of these strains, which are of lower virulence than the Wilmington strain.

RAYNAL (p. 59) once more argues his theory that in Shanghai the rickettsiae of murine typhus are spread by fleas from rats to man, and thence from man to man by lice. He names the common rats and their fleas. But in addition, during the war, true louse-borne typhus was introduced from outside, and resulted in epidemics. Murine typhus has been detected in cats in Shanghai, and RAYNAL (p. 251) refers to the possible danger of infected cats to man.

Most of the 184 cases of typhus in two hospitals in Chengtu appear to have been of the flea-borne type (LIU *et al.*, p. 325).

ESKEY and HEMPHILL (p. 990) show that murine typhus in the United States is found chiefly in the south. The months of highest prevalence are July–September, and the numbers of cases reported have increased almost every year since 1913, perhaps because the disease is now more generally recognized. Typhus of murine origin is spread uniformly in Florida, U.S.A., and the rural population is nearly as heavily infected as the urban ; RICKARD and RILEY (p. 780) estimate that two-thirds of the patients reported in 1944–1946 acquired

infection in their homes; most of the others were probably infected at their places of business, especially those concerned with food handling. In Texas IRONS *et al.* (p. 780) showed that almost all urban establishments examined harboured rats with positive complement-fixation tests for typhus, and that 77 per cent. of farms examined also harboured such rats. The disease is evidently widespread in rats, and these rural areas must be included in control schemes. DAVIS (p. 888) shows that the complement-fixation test was positive in 34·7 per cent. of *R. rattus*, and 51·4 per cent. in *R. norvegicus* in a town of Texas. Rats from grain mills were more frequently positive than others.

COLE and KOEPKE (p. 421) discuss the interpretation of the data of rodent ectoparasite surveys, and give in detail the results of surveys in Honolulu, Georgia and Alabama. The long paper contains analyses of large surveys of rats, their fleas and mites, and for these the original should be consulted. The work has a bearing on flea-borne typhus.

CALERO (p. 702) reports an outbreak of typhus of murine origin in Panama city. The patients had all worked in a food store.

A long description of the characters of a strain of murine typhus rickettsia is given by BALTEANU and CONSTANTINESCU (p. 1078).

WEI and WEI (p. 62) have infected silkworm pupae with murine typhus rickettsiae. VARELA and MAZZOTTI (p. 251) show that the armadillo and the field rat are susceptible to murine typhus.

Rats become more susceptible to typhus than normal if they are given a diet low in protein, or in certain vitamins of the B group (pantothenic acid, riboflavin, thiamin). FITZPATRICK (p. 781) shows that reduction of the amount of certain other substances does not have the same effect.

NYKA (p. 325) reports a close study of the histological changes in the lungs of rats inoculated by the nasal route with murine rickettsiae, and of the development of the rickettsiae themselves.

In a typhus control programme in the southern United States (relating to flea-borne typhus of murine origin), the method adopted was to apply 10 per cent. DDT to rat runs, burrows and harbourages. WILEY (p. 423) shows that there was a very considerable reduction of human cases in the dusted areas, compared with the incidence in former years, and that the numbers of *X. cheopis* have greatly diminished.

Proteus OXK type: Vector, mite

The War Office has reproduced, in mimeograph form, a series of reports by AUDY and his colleagues (p. 62) on investigations on scrub typhus in south-east Asia. The work was done largely at the Scrub-Typhus Research Laboratory, Imphal, in 1945–46. There are papers on the outbreaks which occurred, and on the work of the Medical Research Council Scrub-Typhus Commission (the latter by Dr. R. LEWTHWAITE). The second part consists entirely of illustrations, but the third part comprises 22 appendices, of which several by AUDY, PARKER, KALRA, RADFORD and BROWNING, deal with epidemiological subjects, including accounts of outbreaks in India, Ceylon and the Maldive Islands. Some of these have already been noticed in this *Bulletin*. Four appendices deal with subjects relating to the various mites, especially *Trombicula deliensis*, which may be a variant of *T. akamushi*. Several appendices refer to bacteriological and serological aspects of the subject, and a few to the survey methods adopted. It is not possible to condense these important papers further; they cover a very large field, and form a most important record. The original abstracts give much information on their contents.

In a review of knowledge of scrub typhus gained during the war, PHILIP (p. 991) refers to the fact that it might have seriously interfered with the campaign had not quick and effective measures of control been devised. He

points out that larval mites do not ingest blood, but only lymph and tissue fluids, and that they do not remain attached to animal hosts for more than 3–4 days. The chief reservoirs of infection are the mites themselves (as also are the ticks of tick-borne typhus), and the vertebrate hosts are only transitory reservoirs [but see FOX, below]. There is evidence of much difference in virulence in different areas; case-fatality rates varied from 0·6 to 35·3 per cent. in different outbreaks.

SAYERS and HILL (p. 593) report on the fevers of the typhus group in South-East Asia Command during 1941–44. There were about 5,500 cases, of which more than 90 per cent. were of mite-borne typhus, and a small proportion of tick-borne or possibly flea-borne disease.

SAVOOR & DAS MENON (p. 781) diagnosed four cases of scrub typhus in persons who had not been away from Bombay City for four weeks before the attack. *R. orientalis* was isolated from one. Infection was probably acquired from mite-infested coarse vegetation, or from the handling of vegetables. SOMAN (p. 701) reports on the Weil-Felix reaction in Bombay, where the response is usually of the *Proteus OX19* type, though cases of *OXK* reaction are seen. In comment, MEGAW points out that the tick-borne disease may give the *OX19* response. SOMAN and DAS MENON (p. 890) also report cases in Bombay in which the reaction was of *OXK* type, and the rickettsiae of *R. orientalis* type.

LIU *et al.* (p. 1079) report 6 cases of the *Proteus OXK* type from north-west China. Previous records of this form in China have been rare.

RIGHTS and SMADEL (p. 702) have shown that resistance provoked by various strains of *R. orientalis* is not necessarily valid for heterologous strains.

The Moroccan rodent *Meriones shawi* is susceptible to intraperitoneal inoculation of *R. orientalis* (NOURY, p. 889).

DAVIS *et al.* (p. 70) refer to the recovery of 85 strains of *R. orientalis* in Assam and Burma, and to the demonstration of the actual presence of rickettsiae in the tissues of a rat experimentally infected by laboratory-reared offspring of infected mites. FOX (p. 889) has recovered *R. orientalis* from the tissues of infected Swiss mice as long as 610 days after experimental infection, and in cotton rats up to 269 days. The blood was also positive, but for shorter periods. He comments on the significance of these findings in relation to the rodent reservoir of tsutsugamushi disease.

KALRA (p. 70) has observed intracellular inclusion bodies in association with intraperitoneal infection of mice with *R. orientalis*.

The incubation period of tsutsugamushi disease in North Queensland is about 13±2 days. SOUTHCOTT (p. 251) noted that most of the eschars were on exposed parts of the body, which suggests that dibutyl phthalate should be used in prevention. There is evidence that birds are important in spreading the mites, and lizards in maintaining them.

An account of scrub typhus in 68 patients in North Burma is given by REDDY (p. 71); he diagnosed the disease only if the *Proteus OXK* titre rose to 1 in 320, and he notes that in the first week most of the patients showed a positive Widal reaction at 1 in 160 or 1 in 320.

FOX and PETERSON (p. 592) have found that certain thionine dyes have an action in infections of mice with *R. orientalis* and *R. mooseri*.

SNYDER and MORTON (p. 252) have found that a mixture of equal parts of benzyl benzoate and dibutyl phthalate is almost as good as, and rather more persistent than, benzyl benzoate alone, for the impregnation of clothing to protect against mites. Benzyl benzoate itself is rather more effective than dibutyl phthalate. HORTON *et al.* (p. 593) report toxic effects from benzene hexachloride impregnated in garments as a protection against mites, to such an extent that it can be used safely only in such low concentrations as to

eliminate any advantages as an insecticide it might possess over other compounds.

Benzene hexachloride at the rate of 6 lb. per acre is lethal to mites for three weeks or more. LINDUSKA and MORTON (p. 326) have used it from aircraft, or applied by hand, in trial plots of land. The object was to find a means of preventing scrub typhus by destroying the vectors before the land is used for camping.

Indeterminate type : Vector, tick

BETTINARDI (p. 423) has written a critical summary of the extensive literature of the tick-borne typhus of the Mediterranean. PARTELIDES (p. 327) reports a case which he diagnosed as boutonneuse fever in Cyprus. COMBIESCO (p. 1080) has isolated rickettsiae from *R. sanguineus* in Rumania, where boutonneuse fever occurred.

FINDLAY and ARCHER (p. 782) report three cases diagnosed as tick-borne typhus, in European soldiers in West Africa. Serological tests indicated affinity with South African tick typhus, but not with louse-borne or flea-borne typhus. DICK and LEWIS (p. 328) describe a rickettsial disease in troops and prisoners of war in East Africa, which they think was transmitted by ticks (*Rhipicephalus simus* and *Haemaphysalis leachi*). Similar cases were being reported from many areas at the same time. SFORZA (p. 890) has isolated strains of epidemic and murine typhus rickettsiae in Eritrea. He has also isolated strains from the ticks *Rhipicephalus sanguineus* and *R. appendiculatus*. He describes an outbreak of tick typhus, which is closely allied to boutonneuse fever. Some of the dogs in Asmara give Weil-Felix reaction of *OX19* or *OX2* type, at high titres (SFORZA and SOLINAS, p. 890).

STREETEN *et al.* (p. 891) report tick typhus from Queensland ; in some of the cases the Weil-Felix reaction was positive in high titre to *Proteus OX19*.

In Mexico epidemic and murine typhus, and Rocky Mountain spotted fever are known to occur. BUSTAMANTE and VARELA (p. 165) note that *Rhipicephalus sanguineus* and *Amblyomma cajennense* are the vectors of spotted fever. These authors (p. 252) produced typical Rocky Mountain spotted fever in guineapigs inoculated with material from *R. sanguineus* collected from various parts of Mexico.

KELSEY and HARRELL (p. 1079) discuss the treatment of Rocky Mountain spotted fever in children ; there is an indication that hyper-immune rabbit serum may be useful if given during the first 3 days. With a dose of 0·33 to 0·5 gm. *p*-aminobenzoic acid per lb. body weight in children suffering from Rocky Mountain spotted fever, TICHENOR *et al.* (p. 326) maintained a blood level of 15–40 mgm. per cent. This treatment was continued for about 7 days, and the results indicated beneficial action in 6 of 8 cases so treated. For the treatment of Rocky Mountain spotted fever RAVENEL (p. 168) has used *p*-aminobenzoic acid in doses of 0·5 gm. per pound of body weight for large children, or more for small children, to give blood concentrations of 30–60 mgm. per 100 cc.

Serological studies undertaken two years after an outbreak of what was diagnosed as atypical pneumonia have shown that the patients' sera reacted strongly to the complement-fixation test for Q fever. CAUGHEY and DUDGEON (p. 168) therefore think that the outbreak (in Italy in 1945) was Q fever, which was responsible for a number of outbreaks about that time.

COMBIESCO *et al.* (p. 169) have identified a rickettsial disease in man in Rumania, which was probably Q fever. PAYZIN and GOLEM (p. 891) report Q fever from Turkey.

Q fever

GSELL (p. 327) has established the occurrence of Q fever in Switzerland Although the reservoir and the mode of transmission could not be determined, there seems to be an association with cattle and the possibility that infection may be acquired by inhalation of infected dust. An outbreak of Q fever, diagnosed retrospectively by serological tests, occurred in men in Switzerland engaged in unpacking heavy goods from America. WEGMANN (p. 782) thinks that this was due to inhalation of infected dust from the packing straw.

An outbreak of Q fever took place in a Chicago slaughtering establishment; SHEPARD (p. 71) points out that the patients handled the freshly killed animals, and as there was no indication of transmission by arthropods, he thinks that infection was probably acquired by inhalation of infected droplets. SHEPARD and HUEBNER (p. 992) discuss the epidemiology of Q fever (often diagnosed originally as atypical pneumonia) in Los Angeles County. It occurs in cattle, and in people associated with them; *R. burneti* has been found in raw milk. There is no evidence of tick transmission to man. Many cases of Q fever in California were in patients who had close contact with dairies, and 10–20 per cent. of the cattle gave positive complement-fixation tests for Q fever. HUEBNER *et al.* (p. 509) infected guineapigs by injecting pooled milk, though none of the cows giving the milk was ill. Although there is no definite incrimination of milk in human cases, it is possible that it may be a source of infection by some mode yet to be determined.

STRAUSS and SULKIN (p. 783) have found positive complement-fixation tests for Q fever in meat-handlers in Texas; they are probably the result of unrecognized attacks of Q fever. The same authors (p. 783) note that the complement-fixing antibodies tend to persist for many months after clinical attacks of the disease.

EKLUND *et al.* (p. 71) describe a case of Q fever probably contracted by exposure to ticks in nature in Montana, perhaps through crushing them against the skin.

BLANC *et al.* (p. 892) used Q fever therapeutically in cases of mental disease. When infected guineapig material was injected intramuscularly a short fever resulted, but injection of infected ticks caused a longer spell of fever. Intradermal injection gave a local reaction, and very slight fever (in two patients out of 10). Nasal instillation also gave slight fever except in two who inhaled heavy suspensions; they, and also two attendants who wore masks, developed pulmonary manifestations.

Streptomycin is rickettsiostatic, and HUEBNER *et al.* (p. 594) have found that it is effective in treatment of guineapigs infected with *R. burneti*, but the treatment was started much earlier than would be possible in human Q fever. Successful treatment of Q fever with streptomycin is reported by ROSOVE *et al.* (p. 892).

SMADEL *et al.* (p. 424) have prepared yolk-sac vaccines of the rickettsia of Q fever, but have had no opportunity to test them in man.

Trench fever

ASCHENBRENNER (p. 783) reviews the literature on trench fever.

BIELING and OELRICHS (p. 893) found that Russian prisoners of war employed as donors of blood to clean, laboratory-bred lice, infected them with *R. quintana*, although the prisoners had not been exposed to infection for 2–3 years. The infectivity was not associated with recrudescence of symptoms of the disease. The same authors (p. 892) show that serum of human convalescents from trench fever inhibits *R. quintana*, and that this can form the basis for a Giroud test.

Rickettsialpox

The initial lesion of rickettsialpox resembles that of scrub typhus, and the rash is similar to that of other rickettsial diseases, except that vesicles occur (DOLGOPOL, p. 703).

An account of rickettsialpox has been written by GREENBERG and PELLITTERI (p. 71). *Charles Wilcocks*

MALARIA

DE OLIVEIRA, C. G. & FREIRE, F., Jr. Uma epidemia de malária inoculada. [**An Epidemic of Inoculated Malaria.**] Reprinted from *Bol. Clin. Hosp. Civis Lisboa.* 1948, v. 12, No. 4, 32 pp. [20 refs.] English summary.

This is the report of a thorough investigation of a remarkable outbreak of *P. falciparum* malaria in Lisbon.

In February and March, 1946, two patients were admitted to hospital apparently suffering from malignant jaundice consequent upon neosalvarsan treatment of the syphilis from which they were suffering. Investigation showed that they were both suffering from *P. falciparum* malaria ; both had anaemia and jaundice and one had cerebral symptoms. Two weeks later a third similar case was admitted. None of the three men had ever left Lisbon ; *P. falciparum* malaria is not indigenous in Lisbon. The three men had all been undergoing treatment for syphilis in the same out-patient department.

One hundred and eighty-nine patients out of the 297 who had attended the venereal disease clinic during December and January were traced and examined. Twenty-five further *P. falciparum* infections were discovered. Thus there were 28 cases in all ; six patients died.

The source of the infection appears to have been the regurgitation of blood into the syringe during the injection of neoarsphenamine into a sailor who had contracted both malaria and syphilis in Portuguese Guinea in the previous September. Thus the stock solution of the drug in use on that day became contaminated. This may have happened on two occasions, December 10th and January 17th. *Norman White*

ZOLTAI, N. A malária helyzet alakulása Magyarországon és a védekzés lehetöségei. [**Malaria in Hungary and its Prevention.**] *Népegészségügy.* Budapest. 1949, May 1, v. 30, No. 9, 281–7, 3 figs. [14 refs.] French summary p. 304.

For many years, malaria in Hungary had become a "*maladie acclimatée*", but its exact distribution was not worked out until the beginning of the present century. Special studies were undertaken by the parasitology department of the Hungarian Institute of Public Health from 1930 onwards.

Before the last war, there were only two epidemic foci, in the north-east and south-west respectively : in other departments malaria, where it existed at all, was only sporadic. The vectors are *Anopheles maculipennis* var. *typicus*, *messeae* and *atroparvus*.

From 1933 to 1936, the number of cases notified annually did not exceed 2,000. In the next five years the yearly average was about 5,000 and in 1942 it exceeded 7,000. The climax of malarial morbidity was reached in 1943, when 8,338 cases were reported. The author believes, however, that the number of cases notified represents only about one-tenth of the real total, which he puts at 80,000 to 100,000 per year. Most of the infections are caused by *P. vivax* and about 10 per cent. by *P. falciparum*.

The direct mortality caused by malaria in Hungary is minimal. The principal importance of the disease is that it reduces general resistance and it has serious economic consequences in taking people away from their agricultural work during the summer.

After the war years of 1944–45, the malaria position in Hungary underwent a fundamental change. As a result of large-scale movements of troops and civilians, indigenous strains became widely diffused and new strains were introduced from outside. A large number of new foci were created and malaria appeared in many districts where it had not been known before or where it had been very limited. These new foci now accounted for about half the cases notified, although previously the majority of cases had been reported in the two original foci referred to above.

These new conditions aggravated the serious economic consequences and antimalarial work was intensified. Besides free drugs distributed by the Institute and the extension of general control work on breeding grounds and water sources, experiences with DDT in 1947 have promised excellent results.

The distribution of malaria in Hungary is shown in two maps, a chart and a table. *H. J. O'D. Burke-Gaffney*

MALMEJAC, R. Rapport sur l'épidémie de paludisme sévissant en 1946 dans le département d'Oran. [**Epidemic of Malaria in 1946 in the Department of Oran.**] *Algérie Méd.* 1947, Mar., No. 3, 259–63.

A very severe outbreak of malaria occurred in the Department of Oran in 1946, more especially in the east and south-east. The previous three years had been dry and there had been a steady regression of malaria incidence. Insufficient treatment of cases, insufficiency of gametocidal drugs and the arrival in the Department of infected workers from Morocco ensured widespread sources of infection. Antilarval measures were altogether inadequate ; abundant spring rains caused a multiplicity of anopheline breeding places. The susceptible population was increased by the arrival of nomads from the high plateaux, in large numbers. The resistance of the indigenous population had been weakened by successive epidemics of typhus and relapsing fevers.

Pernicious forms of malaria were unusually prevalent and the fatality rate was high. *P. vivax* and *P. falciparum* infections were both numerous, the latter appearing in September. Pernicious attacks of *P. vivax* malaria were commonly seen.

The author concludes with an urgent plea for the expansion and intensification of antimalaria work in the Department. *Norman White*

SCHWETZ, J., BAUMANN, H. & FORT, M. Contribution à l'étude du paludisme endémique dans le district du Kwango. (Troisième note.) [**Contribution to the Study of Endemic Malaria in the Kwango District.**] *Ann. Soc. Belge de Méd. Trop.* 1948, Dec. 31, v. 28, No. 4, 421–8.

The authors report the results of the examination of thick drops and smears of blood from 167 children under two years of age living in villages near Feshi in the Kwango District of the Belgian Congo. Malaria has been less studied in this District than in others ; a previous report was published in 1938 [this *Bulletin*, 1939, v. 36, 778]. Feshi lies to the east of the area previously studied.

Malaria parasites were found in 53·2 per cent. of these children under two years of age. *P. malariae* was found in 14 children, in association with *P. falciparum* in all cases but one. *P. vivax* was not found. Gametocytes of *P. malariae* were noted in 14 and crescents in 38 films. For the most part the parasite densities were not high. *Norman White*

GARNHAM, P. C. C. **The Incidence of Malaria at High Altitudes.** *J. National Malaria Soc.* 1948, Dec., v. 7, No. 4, 275–84, 4 figs. [13 refs.]

A discussion of recent literature concerning the occurrence of malaria at unusually high altitudes is followed by an interesting account of the manner in which malaria has in recent years crept higher and higher into the hitherto healthy highlands of Kenya and adjacent territory. The extension of the disease follows the gradual development of the country. Motor and rail transport bring the mosquito from the low-lying hyperendemic areas. Wheel ruts in rough cart roads make ideal pools for the breeding of *A. gambiae.* The construction of roads and rails generally implied borrow pits. Dams on rivers interfered with natural drainage. Imported labour provided reservoirs of infection. During the war conditions were intensified by increased movements and the erection of military camps. Fortunately the malaria transmission season at high altitudes is short, the higher the shorter, and the density of the vector species is very low.

In the highlands of Kenya *P. falciparum* is chiefly responsible for epidemics : *P. vivax* is occasionally seen ; *P. malariae* is comparatively rare. The outbreak begins in May or early June, reaches its height in June or July, and declines in August.

The normal anopheline fauna of the highlands, *A. ardensis*, *A. natalensis*, *A. garnhami*, *A. cinereus*, *A. kingi*, and *A. christyi* are not natural malaria carriers. The introduction of *A. gambiae* or *A. funestus* into the highlands is the cause of the trouble. These dangerous vectors cannot breed if the mean atmospheric temperature is below 61°F. At 2,250 metres this temperature occurs during only four months of the year : at 2,700 metres this temperature is never attained.

A temperature of 64·4°F. is necessary for the development of *P. falciparum* in the mosquito. This temperature is rarely reached in the highlands, but *A. gambiae* and *A. funestus* spend most of their lives in human habitations. The temperature in small native huts is usually at least 5°F. warmer than outside.

The use of an insecticide such as DDT should be effective in controlling these highland epidemics : if it failed to kill all the resting adult mosquitoes it would drive them out of doors where sporogony would cease [see also this *Bulletin*, 1945, v. 42, 959 ; 1949, v. 46, 10]. *Norman White*

BUSTOS CASTELLANOS, J., CERDÁN MURRIETA, L., LASSMAN, G. & ORTIZ, Carmen. **A Malaria Reconnaissance of the State of Veracruz, Mexico.** *Amer. J. Trop. Med.* 1949, Jan., v. 29, No. 1, 23–35, 6 maps.

This malaria survey was carried out jointly by the Ministry of Health of Mexico, the Veracruz State Health Service, and the International Health Division of the Rockefeller Foundation between 1944 and 1946.

The State of Veracruz is on the east coast of Mexico along which it stretches for 960 kilometres. Its width varies from 47 to 212 kilometres. Most of it is hilly or mountainous, except for the coastal plains. Wet and dry seasons are sharply defined ; the rains usually last from May to October. The population, 1,775,274, is largely Mestizo. The State is predominantly agricultural.

During the survey, schools were visited throughout the State where children were examined for enlargement of spleen, and blood films were taken. Spleen rates and parasite rates are much lower at altitudes about 1,000 metres, where the predominance of *P. vivax* over *P. falciparum* becomes more marked. Only a few small towns had a spleen rate over 50 per cent. and the State as a whole can be considered as a zone of moderate malarial endemicity.

More than a thousand collections of adult mosquitoes and larvae were made and some 46,000 specimens identified. *Anopheles albimanus* is the predominant species up to an altitude of 1,100 metres ; it is most prevalent at the end of the rainy season. *A. pseudopunctipennis* is most abundant in the dry season ; it is found up to an altitude of 1,500 metres. It is probable that *A. albimanus* is the chief malaria vector ; *A. pseudopunctipennis* and *A. quadrimaculatus* must also be considered. *A. punctimacula* and *A. vestitipennis* were also captured in dwellings and may transmit malaria. The remaining seven species of anophelines identified were much less abundant and were rarely found in houses. *A. parapunctipennis* occurs in zones where malaria is absent. The natural infection rates of the Veracruz anophelines and their host preferences have not yet been adequately investigated. A DDT spraying programme is now being developed in the State.

The northernmost distribution limits of the following neotropical anophelines of the northern hemisphere are found in the State of Veracruz : *A. argyritarsis*, *A. punctimacula*, *A. apicimacula*, *A. neomaculipalpus*, *A. eiseni*, *A. vestitipennis*, *A. strodei*, *A. parapunctipennis* and *Chagasia bathanus*. *Norman White*

THONNARD-NEUMANN, E. & STAHLMANN, W. Die Infektion jugendlicher Erythrocyten durch das *Plasmodium vivax*. I. Mitteilung. [**Infection of Young Erythrocytes by** *Plasmodium vivax*.] *Klin. Woch.* 1948, July 15, v. 26, Nos. 27/28, 423–4, 1 chart. [11 refs.]

In a previous paper [this *Bulletin*, 1946, v. 43, 520] one of the authors confirmed the findings of other observers, that *Plasmodium vivax* had a predilection for reticulocytes. The present paper describes further observations on this question, carried out in four cases of induced benign tertian malaria. The red blood corpuscles were examined in moist-chamber preparations, stained supravitally with brilliant cresyl blue and counterstained by Pappenheim's method. It is emphasized that the blood should be taken within 3 hours from the onset of fever, since later the reticulocytes are transformed into erythrocytes and it is impossible to determine which of the latter cells were invaded while still immature. In making the counts only cells harbouring young parasites were taken into consideration. In the course of 21 observations it was found that from 12 to 70 per cent., and on the average 32·8 per cent. or one third of the parasites were in reticulocytes. Comparative counts of erythrocytes and reticulocytes harbouring young parasites showed that from 0·008 to 1·3 per cent. of the former and from 1·4 to 29 per cent. of the latter were infected. The ratio of infected reticulocytes to infected erythrocytes was invariably above 1, usually fluctuating between 14 and 500, the average being 97. The preferential invasion of the reticulocytes was also evident from the fact that on the average only 13 of these cells to every 1,000 erythrocytes were present in the blood.

However, in various cases and at different periods of the same infection, the occurrence of the parasites in reticulocytes and in normocytes was subject to fluctuations. It was found that more reticulocytes are attacked during the latter phase of the disease than at the beginning, the increase being especially marked in the third week of the disease, when there is a spontaneous decline in the infection. The decrease in the number of parasites in the circulation is followed by multiplication of the reticulocytes, which are then attacked by the surviving parasites causing a new rise in their number. The author was able to repeat this phenomenon experimentally, by treating a patient with small doses of neosalvarsan, when suppression of the parasites was followed by an increase in the number of parasitized reticulocytes.

The cessation of fever, accompanied by a drop in the number of parasites, in the third week of the disease is regarded as the first sign of acquired immunity. The subsequent invasion of the reticulocytes is said to represent a reaction on the part of the parasites against the defence forces of the host, affording protection which enables them again to increase in numbers and bring about a new febrile paroxysm. *C. A. Hoare*

OMORI, N. **Observations on the Nocturnal Activities of the Anopheline Mosquitoes in Taiwan. I. Preliminary Report.** *Acta Nippon. Med. Trop.* Taihoku. 1942, v. 4, Nos. 1/2, 59–67, 2 pls. [11 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1949, Mar., v. 37, Pt. 3, 38–9.]

An account is given of studies carried out in 1939–40 on the nocturnal activities of Anopheline mosquitoes in a village in Formosa situated at the foot of the mountains, 500 ft. above sea level. There were irrigated rice-fields and streams of running water in the neighbourhood, and the people kept cattle, pigs and poultry. A bait trap of mosquito nets, of the type described by Gater, was used in the studies. A man occupied it from sunset onwards, and collections were made every hour or two hours by means of a chloroform tube and an electric hand lamp. The observations were made on nine occasions, covering every season except spring, the trap being indoors on rainy nights and outdoors in fine weather. The mosquitoes were comparatively inactive when it was cold, rainy or cloudy. Results are shown in tables. Considerable numbers of mosquitoes entered the trap throughout the night in July whereas their activity decreased considerably after midnight in October. This was probably on account of the higher temperature in July as well as an hour's difference in the time of sunset. The species could be roughly divided into three groups. The first, comprising *Anopheles maculatus*, Theo., *A. annularis*, Wulp, *A. hyrcanus* var. *sinensis*, Wied., and possibly *A. tessellatus*, Theo., began to enter the trap just after sunset; their numbers reached a peak in 2–3 hours, diminishing gradually until midnight and very rapidly thereafter. The second, consisting of *A. minimus*, Theo., and possibly *A. splendidus*, Koidz., showed increased activity about midnight; and the third, comprising *A. jeyporiensis* var. *candidiensis*, Koidz., maintained sporadic activity through the night, showing no definite pattern. Two females of *A. ludlowi*, Theo., were also taken. *A. annularis* was by far the most abundant species, and *A. minimus* and *A. maculatus* were next in order of frequency, the total numbers taken being 2,151, 184 and 179, respectively. *A. minimus* has been considered the principal vector of malaria on the island, followed by *A. maculatus*, but in view of its numerical predominance, the author considers that *A. annularis* should be taken into account. Notes are also given on the results of collections of larvae from streams and other water near the village. *A. annularis* and *A. maculatus* were most frequently taken, and larvae were also found of *A. ludlowi*, *A. aitkeni* var. *bengalensis*, Puri, and *A. lindesayi*, Giles, species that were not attracted to man, and of *A. hyrcanus* var. *sinensis* and one each of *A. splendidus* and *A. minimus*.

PENN, G. H. **Pupae of the Nearctic Anopheline Mosquitoes North of Mexico.** *J. National Malaria Soc.* 1949, Mar., v. 8, No. 1, 50–69, 14 figs. [16 refs.]

KAHN, R. L. **Universal Serologic Reaction with Lipid Antigen. V. In Malaria.** *Amer. J. Clin. Path.* 1949, May, v. 19, No. 5, 414–18, 4 figs. [Summary appears also in *Bulletin of Hygiene*.]

For the study of the universal reaction in malaria, nine volunteers were inoculated with *Plasmodium vivax* and their sera were tested before inoculation,

and at various periods after inoculation In one case, which was fairly typical of all, the results were as follows :—(1) before inoculation limited precipitation in Zone I especially after 4 and 24 hours' incubation at 5°C., none in Zone II, slight in Zone III after 4 hours and moderate after 24 hours ; (2) 15 days after inoculation (when fever was subsiding and parasites becoming fewer), results much the same as in (1) ; (3) 29 days after inoculation, considerable precipitation without incubation and further precipitation after 4 and 24 hours ; (4) 2 months after inoculation, precipitation much decreased ; (5) 4 months after inoculation, results similar to (1). Thus the malarial reaction occurred approximately one month after inoculation, 20 days after the beginning of the fever and about a fortnight after its subsidence : the reaction tended to return to normal after about 2 months. It is not suggested that the above results have any practical application but they may be compared with those obtained in certain other diseases.

T. E. Osmond

DE GRAAF, W. Over het recidiveren van malaria. [**Concerning Malaria Relapses.**] *Nederl. Tijdschr. v. Geneesk.* 1949, June 4, v. 93 (ii), No. 23, 1849–60. English summary.

In a prisoner of war camp in Batavia there were collected in the course of three years, 654 cases of malaria. The disease did not occur normally in that area, so that it was possible to watch relapses without the complication of new infections. There were three main groups :—

1. The Timor group, consisting mainly of incompletely treated Australian troops. They mostly had benign tertian infections.
2. The Flores group consisting of Dutch troops very heavily infected, many with mixed benign tertian and subtertian infections, but mostly the former.
3. The remainder—a very varied group.

These patients were carefully watched. Most of the subtertian relapses took place within four weeks and there were none after nine weeks. Of the benign tertian relapses the greatest number, 72 per cent., occurred within a month of the last day of treatment ; 93 per cent. occurred within two months. After two months the number of relapses fell steeply, a fact to be borne in mind in assessing therapeutic and prophylactic measures. The peak of relapses occurred in the third week and the peak observed at seven months by James was not seen in this series.

A number of patients were followed up for many months, some up to three years. Of these 30 had one, 20 two, 7 three, 8 four, 6 five, 2 nine and 1 twelve relapses. A series of relapses could terminate quite suddenly or the interval could gradually increase till they ended or, in some cases, malaria parasites persisted in the blood without causing any clinical manifestations.

No patient continued to have parasites in his blood or to relapse for more than a year and a half.

Among the 85 subtertian cases there were six deaths, but many fewer relapses than among the benign tertian cases.

Therapeutic material was very scarce, but in spite of the difficulties controlled trials were carried out.

The first trials were directed towards economy in quinine. The original dose of 1·2 gm. per day for seven days was reduced to 1·2 gm. for five days (benign tertian cases only) without increasing the relapse rate. A few cases were treated with 1·2 gm. for one day only ; this small dose was apparently quite successful.

Subsequently three forms of treatment were used on patients taken in rotation :

1. Atebrin [mepacrine]—100 mgm. three times daily for five days.
2. Quinine—1·2 g. daily for five days.

3. Quinine as above immediately followed by plasmoquine 20 mgm. three times daily for five days.

The results from atebrin were apparently the worst as judged by relapses, but there were only 18 cases drawn from the most heavily infected group; supplies ran short after these had been treated. There was no statistically significant difference between the relapse rates of the three groups. The only advantage was apparently with the group given plasmoquine, none of whom had more than four relapses. *A. L. Winner*

RAYNAUD, R., MINICONI, P. & CHEVROT, L. Les états méningés du paludisme. [**Meningeal Conditions in Malaria.**] *Algérie Méd.* 1947, Mar., No. 3, 215–21. [16 refs.]

Three groups of meningeal manifestations can be distinguished in malaria infections: (1) meningeal reaction without clinical symptoms; (2) meningitis complicating a more or less typical attack of malaria; (3) malarial meningitis in which the meningeal symptoms mask completely the basic malaria infection. The recognition of the first group depends upon an examination of the cerebrospinal fluid which shows a more or less marked lymphocytosis. This is of frequent occurrence in acute attacks of malaria. It may account for severe headaches, neuralgias, neuritis and paralysis of cranial nerves that are listed among the complications of malaria.

In the second group the involvement of the meninges has objective signs, rigidity of the neck and Kernig's sign, with lymphocytosis and increased albumin in the cerebrospinal fluid. These meningeal signs are superimposed on more or less typical symptoms of malaria.

Malaria meningitis is much rarer. Here meningitis symptoms are alone in evidence. The sudden onset, and the absence of all the usual symptoms of malaria make the diagnosis extremely difficult. It is only in malarious countries that one would consider the possibility of a malarial infection. Lumbar puncture may reveal a normal cerebrospinal fluid in the early stages; later the fluid may become opaque with a predominance of polymorphonuclear leucocytes. In the blood *P. falciparum* is almost always in evidence. In countries in which relapsing fever occurs the differential diagnosis may be further complicated; an attack of relapsing fever may be ushered in with meningeal symptoms.

The authors describe cases illustrative of each of these three groups of meningeal manifestations in malaria. *Norman White*

RAYNAUD, R., MINICONI, P. & CHEVROT, L. Un cas de méningite palustre. [**A Case of Malarial Meningitis.**] *Algérie Méd.* 1947, Mar., No. 3, 233–5.

A woman aged 33, after a few days of malaise, loss of appetite and slight fever, suddenly lost consciousness and was admitted to hospital. She presented a psychic disturbance which was attributed to alcoholism: her temperature was 39°C. The following day she was found to be in a state of complete coma with a temperature of 41°. She presented a typical meningeal syndrome muscular hypertony, rigidity of the neck, and Kernig's and Brudzinski's signs. The tendon reflexes were active; the light reaction of the pupils was normal. Lumbar puncture showed a clear cerebrospinal fluid. The signs of meningitis were so unequivocal that intramuscular injections of penicillin and Soludagenan, alternately, were commenced without delay. The temperature fell but the nervous symptoms were aggravated. The following day the laboratory reported the presence of *P. falciparum* in the blood. Quinine treatment procured a rapid recovery though the psychic disturbance persisted for three or four days.

Norman White

BENHAMOU, E., ALBOU & LEONARDON. Les facteurs de pronostic dans l'accès pernicieux. [**Factors of Prognostic Significance in Pernicious Attacks of Malaria.**] *Algérie Méd.* 1947, Mar., No. 3, 238–45.

A study of 55 cases of pernicious *P. falciparum* malaria have led the authors to the conclusion that prognosis cannot be based on any single sign such as the depth of the coma, the intensity of anaemia or the urea content of the blood, but that a combination of signs may afford a guide. The duration of coma before the institution of treatment is of great significance. The combination of high blood urea, coma, and high parasite density is a grave omen. If the complement content of the blood falls to and remains at zero an early fatal result may be expected.

Recovery from a pernicious attack may leave the patient very susceptible to serious secondary infections to prevent which the authors recommend treatment with very large doses of penicillin. *Norman White*

BRUCKNER, Sylvia & LĂZĂRESCU, Mircea. Sindrom encefalitic in cursul malariei cronice. [**Encephalitic Syndrome in Chronic Malaria.**] *Rev. Ştiinţelor Med.* Bucharest. 1948, Nov.–Dec., v. 37, Nos. 11/12, 625–31. [15 refs.] French summary.

The following is a translation of the authors' summary :—

After reviewing the various nervous complications of malaria the authors describe two cases with encephalitic features appearing in the chronic stage of *P. falciparum* infection.

Attention is drawn to the pathological anatomy, the pathogenesis and the importance of aetiological diagnosis in such nervous cases.

H. J. O'D. Burke-Gaffney

PÉTA, T. Sul significato e l'origine delle emorragie petecchiali nei soggetti malarici. [**Significance and Cause of Petechial Haemorrhages in Malaria Patients.**] *Riv. di Malariologia.* 1948, Aug., v. 27, No. 4, 171–8. [19 refs.] English summary (5 lines).

The author describes eight patients, all from Matemma or Gallabat, Asmara, who were suffering from malaria and who had petechiae on the trunk or limbs or both. Though malaria may cause haemorrhagic lesions in severe infections, good evidence is produced that the petechiae in the cases in question were due to a deficiency of vitamin C in the inadequate diet. *Norman White*

HENRY, A. F. X. De la sérologie palustre à la thérapeutique du paludisme chronique. [**Serology in the Treatment of Chronic Malaria.**] *Bull. Acad. Nat. Méd.* 1949, v. 133, Nos. 9/10, 193–6.

——. Les bases biologiques du traitement des formes prolongées de l'infection palustre. [**Biological Bases of the Treatment of Prolonged Forms of Malaria Infection.**] *Ibid.*, 196–8.

——. Quelques directives pour le traitement du paludisme subaigu et du paludisme chronique. [**Suggestions regarding the Treatment of Subacute and Chronic Malaria.**] *Ibid.*, 198–201.

The author enlarges on the value of the melano-flocculation reaction which bears his name, during the treatment, as well as in the diagnosis, of malaria infections.

Chronic malaria is a general, focal and organic disease characterized above all by a deficient oxygen supply to tissues with all the damage that such a state of affairs may produce. Internal secretory glands and reticulo-endothelial tissues are specially involved. Treatment should have one of two ends in view. If the patient can leave his malarious environment the aim should be the total eradication of the infection, not always easy to obtain. In other circumstances the aim should be the restoration of a state of premunition in which the patient tolerates his infection with impunity.

The author's methods for the catalytic premunotherapy of subacute and chronic malarial infections have been previously described [see this *Bulletin*, 1948, v. 45, 756]. *Norman White*

HERING, E. R., PATT, H. M. & LEAVITT, H. J. **Tolerability Studies of some New Antimalarial Drugs.** *J. National Malaria Soc.* 1948, Dec., v. 7, No. 4, 322–9, 3 figs.

This experiment was designed to test the tolerability, or acceptability, of four of the newer antimalarial drugs of suppressive value, as compared with quinacrine [mepacrine] and a placebo (lactose). Nine hundred and fifty-five volunteer marine recruits were the subject of experiment. The value of the drugs as suppressants was not an object of the study. The drugs tested were given once a week; these drugs, and their weekly doses, were: SN-6911, 0·6 gm.; SN-7618 [Chloroquine], 0·3 gm.; SN-8137 [Oxychloroquine], 0·6 gm.; SN-11437 [2-metanilamido-5-chloropyrimidine], 2·0 gm.; quinacrine, 0·24 gm. The drugs and the placebo were all given in green-tinted capsules after a mid-day meal. None knew which of the six preparations he was given.

After each drug administration the men were interviewed concerning the results of the previous dose and asked if they had any complaints. All complaints were recorded.

Criteria of tolerability were (*a*) refusal to accept the drug after it had been taken at least once; (*b*) complaints attributable to the drug (number of individuals complaining); (*c*) sick bay admissions during the course of the experiment; (*d*) rifle firing scores achieved during the experiment. The observations lasted six weeks.

Quinacrine was productive of most complaints and refusals to continue. SN-6911 was also significantly inferior to the other three drugs. SN-7618 [chloroquine] was the best tolerated causing almost as few complaints as did the placebo (34 complaints of various symptoms were attributed to lactose !). Motor co-ordination, as reflected by shooting scores, was unaffected by the drugs. *Norman White*

WINCKEL, C. W. F. **The Efficacy of Quinacrine and Quinine in the Treatment of *Plasmodium malariae* Infections.** *Documenta Neerlandica et Indonesica de Morbis Tropicis.* Amsterdam. 1949, Mar., v. 1, No. 1, 93–6, 4 graphs.

The author describes his experience in the treatment of *P. malariae* infections with quinine and quinacrine [mepacrine]. His patients were neurosyphilitics who had been infected, for the most part, by intravenous subinoculation. He compares his results with those obtained by YOUNG & EYLES [this *Bulletin*, 1948, v. 45, 680] who administered quinine in much larger doses and for a much longer period than does the author. He concludes that in cases of quartan malaria the results of treatment with 1 gm. of quinine a day are certainly as good as those with 2 gm. a day. The use of large doses should be abandoned. Symptoms of cinchonism of any severity are thereby avoided. "Quinine, when given in appropriate doses, kills many parasites but not all. A certain

amount of antigen comes into contact with the body cells. This stimulates to enhanced phagocytosis and to the secretion of antibodies. When these are present in sufficient numbers, the surviving parasites are killed off. Quinine should therefore be given in such dosage that the cells are not damaged."

Norman White

CLARKE, G. H. V. **A Case of Mepacrine Dermatitis.** [Memoranda.] *Brit. Med. J.* 1949, July 9, 58.

HILL, E. & AMATUZIO, D. S. **Southwest Pacific Vivax Malaria. Clinical Features and Observations concerning Duration of Clinical Activity.** *Amer. J. Trop. Med.* 1949, Mar., v. 29, No. 2, 203–14, 3 figs. [40 refs.]

Between July 1, 1945 and April 1, 1948, 328 patients with *P. vivax* infections that had been acquired in the south-west Pacific were studied in the Veterans' Hospital, Minneapolis. All had received suppressive mepacrine medication while in the Pacific ; this had usually been discontinued on their return to the United States. Since discharge from the Service all had resided in a non-malarious region of the United States.

Chills, fever and malaise ushered in the attack in almost all cases : other prodromal symptoms were present in 46 per cent. Enlarged spleen was noted in 37·6 per cent. of patients. Anaemia was not a marked symptom ; the patients were well nourished. The haemoglobin level was not related to the number of attacks.

One hundred and sixty-nine patients were treated with mepacrine ; 62 with chloroquine. Mepacrine dosage was 0·2 gm. every six hours for five doses, then 0·1 gm. thrice daily for six days. Chloroquine diphosphate dosage was 1·0 gm. followed by 0·5 gm. six hours later, then 0·5 gm. on each of the second and third days. The relapse rates of comparable groups of patients treated with mepacrine and chloroquine were 60 and 56 per cent., respectively. The relapses after chloroquine treatment occurred much earlier. Chloroquine was in no way more effective than mepacrine. There were no symptoms of toxicity with either drug.

A study of the duration of infection was made in 155 patients, none of whom was treated with drugs likely to eradicate the infection such as quinine-plasmoquine or pentaquine-quinine. Infections were terminated in the first year in 24·5 per cent. ; in the second year in 52·9 per cent. ; in the third year in 18·3 per cent. Attacks were still occurring in the fourth year in 4·3 per cent. All the patients probably harboured multiple strains of Pacific *P. vivax*.

Norman White

CULWELL, W. B., COOPER, W. C., WHITE, W. C., LINTS, H. A. & COATNEY, G. R. **Studies in Human Malaria. XX. The Intramuscular Administration of Chloroquine.** *J. National Malaria Soc.* 1948, Dec., v. 7, No. 4, 311–15. [10 refs.]

Chloroquine was given intramuscularly to 16 young male volunteers who had been infected with the Chesson strain of *P. vivax* by mosquito bite. It was given as the hydrochloride in sterile unbuffered aqueous solution containing 45 mgm. of the salt (40 mgm. base) per ml. The *p*H of the solution was 5·6. Treatment of each attack was begun on the third day of patent parasitaemia if the oral temperature had reached 102°F. by 8 a.m. on that day. Three systems of dosage were used : single injection of 200 mgm. (base) ; two injections of 200 mgm. each, four-hour interval ; single injection of 300 mgm. Injections were made in the gluteal muscles.

The highest plasma concentrations of chloroquine were obtained 15 minutes after injection, in all but four cases. The highest concentration observed in any subject was 480 mgm. per litre. Clinical response was rapid in all cases. There were no toxic reactions.

Where oral administration of chloroquine is not possible treatment can safely be begun by the intramuscular injection of 200 mgm. of base, repeated after four hours if necessary. Treatment by mouth, to complete a course of 1·5 gm. of base in three days should be started as soon as practicable. *Norman White*

GIOVANARDI, A., SEPULCRI, P. & DE NEGRI, U. Il " Palusil " (N^1-p-clorofenil-N^5-isopropil-biguanide) nella terapia della malaria.—Nota II : Effetti del trattamento della malaria naturale da *Plasmodium vivax*. [**Paludrine (Proguanil) in the Treatment of Malaria. Note II. The Effects of Treatment of Naturally Acquired** *P. vivax* **Infections.**] *Riv. di Malariologia.* 1948, Oct., v. 27, No. 5, 191–200, 1 graph. English summary (7 lines).

This is a progress report of an investigation the authors were making on the value of palusil, Italian paludrine [Proguanil], in the treatment of malaria. Three hundred and twenty-three patients suffering from *P. vivax* malaria were treated, 201 from the Province of Venezia and 122 from the Province of Rovigo. The results were satisfactory. Various doses were prescribed. The best results were obtained with 0·3 gm. a day for 15 days followed by the same dose once a week for five weeks. Among 30 patients so treated only one relapsed, on the 20th day after the end of treatment. The reduction in the size of enlarged spleens began after the first day of treatment ; in more than 70 per cent. of the patients treated with palusil the spleens were normal in size after the end of treatment. The drug was generally given after food and was well tolerated.

Blood counts in ten patients with chronic infections showed a marked increase in the number of red cells that resulted from treatment, together with a return to normal of the differential leucocyte count. *Norman White*

WHITE, W. C., COOPER, W. C., COATNEY, G. R., CULWELL, W. B., LINTS, H. A. & YOUNG, M. D. **Studies in Human Malaria. XXI. The Cure of St. Elizabeth Strain** *Vivax* **Malaria by Pentaquine-Quinine, administered during Acute Attacks or during Latency.** *J. National Malaria Soc.* 1948, Dec., v. 7, No. 4, 316–21, 1 fig. [10 refs.]

Fifteen young white male volunteers were infected with the St. Elizabeth strain of *P. vivax* by mosquito bite. This strain produces an infection with a latent period of from 6 to 9 months between the early primary attack and the first relapse. All 15 men developed early primary attacks which became patent 11 to 14 days after the mosquito bites. The men were divided into three groups of five each. On the third to fifth day of patency the men of Group A were treated with concurrent pentaquine and quinine ; the men of Groups B and C were treated with quinine alone. The doses (base) were : pentaquine, 15 mgm. every 6 hours for 14 days ; quinine, 0·5 gm. every 6 hours for 14 days. The acute attacks were alleviated promptly in all cases.

Four months (120 days) after infection the following treatment was given : Group A none ; Group B concurrent pentaquine and quinine ; Group C quinine alone.

The men of Groups A and B had no late attacks of malaria through 18 months of observation. All the five men of Group C developed late relapses 199 to 280 days after the original infection. These late relapses were terminated with pentaquine and quinine and no subsequent attacks developed during the following 18 months.

During the 15 courses of combined pentaquine-quinine therapy the complaints were : abdominal cramps, 14 ; epigastric tenderness, 9 ; nausea, 6 ; anorexia, 4 ; nausea and vomiting, 3 ; tinnitus and dizziness, 5 ; urticaria, 2 ; fine macular rash, 1 ; fine papular rash, 1 ; tremor, 1 ; blurring of vision, 1. Only one man had no complaints.

During the 15 courses of quinine alone the complaints were : abdominal discomfort, 2 ; epigastric tenderness, 1 ; nausea, 3 ; tinnitus, 3 ; dizziness, 5 ; urticaria, 1 ; fine macular rash, 1 ; diarrhoea, 1.

Concurrent pentaquine and quinine have clear-cut curative properties in the treatment of infections with the St. Elizabeth strain of *P. vivax*.

Norman White

GULLAND, J. M. & MACEY, P. E. **Synthetic Antimalarials. Part XXXVIII. 2-(6′-quinolylguanidino)-4-β-diethylaminoethylamino- and 4-(6′-quinolylguanidino)-2-β-diethylaminoethylamino-6-methylpyrimidines.** *J. Chem. Soc.* 1949, May, 1257–9.

CROWTHER, A. F., CURD, F. H. S., DAVEY, D. G. & STACEY, G. J. **Synthetic Antimalarials. Part XXXIX. Dialkylaminoalkylaminoquinoxalines.** *J. Chem. Soc.* 1949, May, 1260–71.

CURD, F. H. S., DAVEY, D. G. & STACEY, G. J. **Synthetic Antimalarials. Part XL. The Effect of Variation of Substituents in 2-Chloro-3-β-diethylaminoethylaminoquinoxaline.** *J. Chem. Soc.* 1949, May, 1271–7.

GAGE, J. C. **Synthetic Antimalarials. Part XLI. Physicochemical Studies on Quinoline Derivatives.** *J. Chem. Soc.* 1949, June, 1458–62, 1 chart.

MATHIESON, D. W. & NEWBERY, G. **Contributions to the Chemistry of Synthetic Antimalarials. Part VIII. Aromatic Carbinolamines.** *J. Chem. Soc.* 1949, May, 1133–7.

KLOPPER, S. **The Suppressive Action of Paludrine in Benign Tertian (Vivax) Malaria.** *Documenta Neerlandica et Indonesica de Morbis Tropicis.* Amsterdam. 1949, Mar., v. 1, No. 1, 50–54, 4 figs.

These carefully controlled observations were made in Wormerveer, a town of 10,500 inhabitants in the Province of North Holland. Paludrine [proguanil] once a week was given to 607 adults and to 566 elementary school children from the middle of April to the middle of July, when malaria is most prevalent : adults received 100 mgm., children 50 mgm., a week. A second group of 510 adults and 474 children received no paludrine but were as carefully observed as the first group. During the period of drug administration the incidence of malaria in the paludrine group was markedly lower than among the control group, the curve falling to zero at the end of May. After the cessation of paludrine the malaria incidence of the treated group rose rapidly, the total malaria morbidity of that group for the season being about equal to that of the general untreated population of Wormerveer. Paludrine delays the clinical attack.

Sixty-four patients who had suffered from one or more malaria relapses in 1946 were each given a tablet a week ; 32 received 100 mgm. paludrine, the remainder sodium bicarbonate. Those who took paludrine regularly had no further relapse during the period of observation : 12 of the 32 patients receiving sodium bicarbonate suffered clinical relapses during this period.

Norman White

HOFFMAN, J. & VAN RIEL, J. Bilan d'un an de lutte antimalarienne par pyréthrage des habitations. [**Appraisal of the Results of a Year's Anti-malarial Work by Treatment of Dwellings with Pyrethrum.**] *Ann. Soc. Belge de Méd. Trop.* 1948, Dec. 31, v. 28, No. 4, 387–94.

In Lenda, a mining settlement of the "*Grands-Lacs Africains*" Mining Company of the Belgian Congo, an experiment to control malaria by dusting dwellings with pyrethrum powder was begun in the middle of May 1947. The settlement was highly malarious. Imported labour recruited in non-malarious localities suffered very severely. *A. gambiae* and *A. funestus* were very abundant ; it was often possible to capture 5,000 or more adults of these species in a single dwelling. The houses were dusted with fresh and finely ground pyrethrum flowers. Dustings were done twice weekly, 40 gm. of powder being used on each occasion for each house. After some months when anophelines could no longer be found the amount of powder used was reduced by half.

The results were spectacular. The infant mortality rate was 210 per 1,000 live births during the first half of 1947 ; it fell to 86 in the second half of that year, and to 52 in the first half of 1948. No such fall was evident in control untreated areas. The mortality rate of older children was 24·3 per thousand during the 12 months preceding the experiment ; it fell to 9·2 during the first 12 months of the pyrethrum treatment.

Previous to the experiment malaria parasites could be found in the blood of infants within a few weeks of birth. After a year of treatment of the camps malaria parasites were found in only one of the 420 infants under one year of age examined.

The rare cases of malaria that are now seen are either relapses or infections contracted elsewhere. *Norman White*

ETHERINGTON, D. **D.D.T. as a Residual Insecticide against** *Anopheles maculipennis*. [Correspondence.] *Nature*. 1949, July 2, 32.

The author refers to Muirhead THOMSON's findings in Africa [this *Bulletin*, 1949, v. 46, 439] that DDT had an irritant effect on *Anopheles gambiae* in houses. The present author had the impression in Italy in 1944–45 that *A. maculipennis* var. *labranchiae* reacted similarly when DDT spraying (5 per cent. in kerosene) was used against "domestic" resting places : it seemed to have a repellent rather than a lethal effect.

He had recorded this experience and its possible implications, with proposals for its investigation, in an official report, but Service conditions precluded the matter being followed up and the series of test experiments which he suggested could not be completed. He points out that Muirhead THOMSON's independent findings with *A. gambiae* support his own earlier observations and he now adds that he considers that the "value of DDT as a malaria control measure is also open to doubt in areas where *A. maculipennis* var. *labranchiae* is the vector". [No experience with Gammexane is recorded.]

H. J. O'D. Burke-Gaffney

DE NEGRI, U. Larvicidi a base di polvere di sughero e di DDT. [**Cork Powder and DDT as a Larvicide.**] *Riv. di Malariologia*. 1948, Oct., v. 27, No. 5, 213–20. English summary (8 lines).

Cork powder, a by-product of the cork industry, consisting of amorphous granules, from 12 to 42 μ in diameter, when applied to the surface of water in quantity not less than 150 gm. per square metre, kills anopheline larvae therein, by asphyxia. The large quantity required precludes its use as a practical larvicide.

If the cork powder be immersed in kerosene containing 5 per cent. DDT—1 kilogramme of powder in a litre of kerosene—the resultant product has a potent larvicidal action against both *Anopheles* and *Culex* when sprayed on water in quantity not less than 25 gm. per square metre. In none of the experiments did this larvicide cause any damage to fish, including *Gambusia*. The low cost of cork as a waste product makes this a cheap way of destroying larvae. *Norman White*

McArthur, J. **Malaria in Borneo. An Account of the Work of the Malaria Research Department, North Borneo, 1939-42.** 250 mimeographed pp., 76 figs. [Numerous refs.] 1948.

A complete account of the investigations discussed in this *Bulletin*, 1947, v. 44, 788.

Haas, V. H., Wilcox, Aimee & Coleman, Nell. **Modification of *Plasmodium gallinaceum* Infections by certain Tissue Extracts.** *J. National Malaria Soc.* 1949, Mar., v. 8, No. 1, 85–99. [17 refs.]

The fact that various laboratory mammals were refractory to *P. gallinaceum* infection suggested to the authors that some substance or substances inimical to the parasite might be present in their tissues. Extracts of various mammalian tissues were therefore prepared and their effect on *P. gallinaceum* was tested *in vitro* and *in vivo*. Since extracts prepared from chickens in a similar way also showed some inactivating effect it appears that a number of other factors are associated with resistance to infection. In the *in vitro* test, with suitable controls, it was found that exposure to saline extracts of pooled mouse tissues inactivated to some extent blood and exoerythrocytic forms of the parasite, also sporozoites as judged by the resulting infection rate in chick embryos inoculated by various routes. Extracts of spleen of various mammals and of chickens affected sporozoites, exoerythrocytic and especially erythrocytic forms of *P. gallinaceum* so that the infection rate in chickens inoculated with these parasites was greatly reduced. Bovine spleen extracts were, however, toxic to chickens, causing necrosis and gangrene at the site of subcutaneous inoculation [the actual site of inoculation of the parasites and extracts is not stated, but if inoculation of both was made at the same spot the necrotic action on tissues mentioned would doubtless affect the injected parasites]. An extract from chicken and bovine blood showed similar properties and toxicity but in lesser degree than those from spleen. It is possible that red or white blood cells present in the spleen were the source of activity. An unsuccessful attempt was made to characterize the active substance, it appeared, however, to be protein. *J. D. Fulton*

Terzian, L. A., Stahler, N. & Weathersby, A. B. **The Action of Antimalarial Drugs in Mosquitoes infected with *Plasmodium gallinaceum*.** *J. Infect. Dis.* 1949, Jan.–Feb., v. 84, No. 1, 47–55, 1 fig.

The present investigation is a continuation of earlier studies by the senior author and Weathersby [this *Bulletin*, 1948, v. 45, 767 ; 1949, v. 46, 609] who indicated that a correlation existed between the activity of prophylactic drugs in *P. gallinaceum* infections of chickens and in infected mosquitoes. Those substances which protected the chicken host against sporozoite infections also arrested oöcyst development in the mosquito, whereas suppressive drugs exerted no such effect. A prophylactic drug in the invertebrate host is defined as one which is effective against presporozoite stages and prevents formation of the latter.

About 100 to 150 *Aëdes aegypti* or *Anopheles quadrimaculatus* were fed on each different concentration of drug prepared in 4 per cent. sugar solution. Mortality was correlated with the level of drug concentration. Feeding on the drug solutions was begun 48 hours before an infective blood meal and continued during the course of infection. Development of oöcysts was followed by dissection of the hosts, and intensity was gauged by their number and that of sporozoites present. Infectivity of sporozoites was tested by inoculation to chickens.

A number of drugs which act as suppressive agents in the vertebrate host including quinine, atebrin (mepacrine), plasmoquine (pamaquin) and others had no effect on oöcyst development or sporozoite production in the mosquito, whereas sulphadiazine, metachloridine [SN 11, 437; 2-metanilamido-5-chloropyrimidine] and paludrine, which are prophylactic in the chicken, prevented oöcyst development and sporozoites were therefore absent. This was found by calculation to be more than a chance relationship and the results confirm the earlier findings of the author. Similar relationships held in the case of *P. falciparum* and its vector *A. quadrimaculatus*. In this case paludrine was the only active drug. The application of these methods to the search for drugs prophylactic in human malaria is obvious, and has the advantage that if levels of drug are adequate effects can readily be judged by mosquito dissection followed by microscopical examination. Photomicrographs of mosquito stomachs taken seven days after an infective blood meal illustrate this fact. It was noted that the effect of prophylactic drugs was exerted late in oöcyst development and the drugs could therefore be withheld for some days after an infective meal and still show activity. A particular phase in the oöcyst developmental cycle appears to be specially vulnerable to drug action. The infectivity of developed sporozoites was not affected except by plasmoquine. The action of metachloridine and sulphadiazine, but not of paludrine was antagonized by para-aminobenzoic acid, and this suggests that the two former substances interfered with the para-aminobenzoic acid metabolism of the parasite, as does sulphadiazine in the case of bacteria. *J. D. Fulton*

KNOPPERS, A. T. **Twofold Quinine Resistance of** *Plasmodium gallinaceum*, **induced by Regular Administration of the Drug.** *Documenta Neerlandica et Indonesica de Morbis Tropicis.* Amsterdam. 1949, Mar., v. 1, No. 1, 55–66. [40 refs.]

The production of strains of avian, monkey and human plasmodia (*P. vivax*) resistant to various antimalarial drugs has been reported in this *Bulletin* from 1942 onwards. The present author described previously a strain of *P. gallinaceum* with two-fold resistance to quinine [this *Bulletin*, 1948, v. 45, 158] of which further details are now given. The method employed was to treat seven-day-old chicks orally with 10 mgm. per kilo of the drug, and to transmit the treated strain by blood inoculation into fresh hosts. At the end of 16 weeks' treatment the dose of quinine was doubled, and after 26 weeks a two-fold resistance was established and could not be increased. The resistance persisted when quinine was withheld for about 26 weeks but was slightly diminished after the first mosquito passage, though not on subsequent passages. Resistance was also shown to cinchonidine and to a lesser degree to cinchonine or quinidine. There was no resistance to atebrin [mepacrine], paludrine [proguanil], chloroquine or sulphamerazine. On the other hand, the strain was more than usually sensitive to pamaquin [plasmoquine], pentaquine and isopentaquine. On passage by means of exoerythrocytic forms, resistance was retained. There is a short theoretical discussion on the significance of these results. *J. D. Fulton*

SICCA, G. T. L'azione del Farma 01015 (Paludrina) sulla infezione da *P. gallinaceum*. [**The Action of Paludrine [Proguanil] in** *P. gallinaceum* **Infections.**] *Riv. di Malariologia*. 1948, Oct., v. 27, No. 5, 201–12. [13 refs.] English summary (3 lines).

This is a record of experiments to determine the efficacy of an Italian preparation of paludrine hydrochloride [proguanil] in the treatment of *P. gallinaceum* infections. Chickens were used. In one group of birds, infection was produced by the injection of 0·2–0·25 cc. of citrated blood, taken from a bird in the acute stage of the infection, into the pectoral muscle. In a smaller group 0·4 cc. of an emulsion of brain tissue of an infected bird in normal saline was injected intramuscularly. All the untreated control birds of less than 120 gm. weight inoculated with infected blood died during the acute phase of the attack; no exoerythrocytic forms were found at autopsy. Some of the heavier birds, from 300 to 550 gm. weight, survived the acute phase to die later during a recrudescence, with exoerythrocytic forms in the internal organs. Most of the birds infected with brain emulsion containing exoerythrocytic forms died during the acute attack with erythrocytic forms in the blood; the acute phase began from 7 to 12 days after inoculation.

Paludrine was given by mouth at different stages of the acute attack. A dose as small as 2 mgm. a day for 3 days had a definite influence in 4 chicks; the high parasitaemia was much reduced, and death was delayed to the 19th to 23rd day after inoculation. Four birds varying in weight from 110 to 400 gm. who were given 5 mgm. a day for 6 days recovered from the infection. One of these was killed on the 63rd day after inoculation: a very few parasitized red cells were found but there were no exoerythrocytic forms.

To test the prophylactic value of the drug, 7 birds inoculated with infected blood received 2 to 5 mgm. paludrine a day for 6 days, beginning 4 hours after the inoculation. These birds were killed at different periods, when the corresponding control birds were suffering from an acute attack or, in two cases, on the 48th and 63rd days after inoculation. In only one living bird were parasites found in the peripheral blood; they were few in number and found on only three consecutive days, 30 days after inoculation. In 2 birds killed on the 16th and 48th day after inoculation a very few infected red cells were found. No exoerythrocytic forms were found in these birds. The experiments confirm the remarkable therapeutic and prophylactic activity of paludrine against *P. gallinaceum*. *Norman White*

CANTRELL, W., KELSEY, F. E. & GEILING, E. M. K. **Sulfonamide Blood Levels in Prophylactic Tests against** *Plasmodium gallinaceum*. *J. Infect. Dis.* 1949, Jan.–Feb., v. 84, No. 1, 32–40.

Certain sulphonamides have been found active in human, monkey and avian malaria. Although the hope was not realized, it appeared probable that a member of the group would be found to act as a prophylactic in human malaria. The experiments described here were undertaken to gain information on the blood levels of drug required to protect chickens from intravenous infection with sporozoites of *P. gallinaceum*. The drugs were given in the diet to chickens kept on a three-hour dark and light schedule. At the end of a light and dark period, blood samples of 0·02 ml. were collected daily or every second day for the determination of sulphonamides, generally in pooled samples, by BRATTON and MARSHALL's method (*J. Biol. Chem.*, 1939, v. 128, 537). Smears were examined for the presence of parasites and inoculation of blood to fresh hosts was used to detect the presence of latent infection in treated birds. In all, 13 experiments were performed in which groups of 5 chickens were given various

drug diets and 5 to 10 chickens served as controls in each case. Protection was afforded by sulphapyrazine, sulphadiazine, sulphamethazine and sulphamerazine in that order, 50 per cent. of the chickens being protected by blood concentrations respectively of 2·6, 3·1, 4·7 and 7·0 mgm. per 100 ml. There was a correlation between the protection afforded and the persistence of drug in the blood. Besides those mentioned, 61 other sulphonamides were tested for prophylactic activity, of which 19 were effective in the doses used, most however being inferior to sulphadiazine in this respect. The disadvantages of the drug diet were that the amount of drug ingested could not be accurately assessed and wide variations occurred in the blood-levels of chickens receiving the same diet. Differences in the rate of disappearance of drugs from blood were also noted. The protective power of the sulphonamides depended on other factors besides blood concentration. Some which failed to protect caused considerable delay in the appearance of the parasites. The relation of structure to activity and drug concentration in the blood is discussed. *J. D. Fulton*

GREENBERG, J. **Hypersensitivity to Sulfadiazine of a Chlorguanide-Resistant Strain of** *Plasmodium gallinaceum*. *J. National Malaria Soc.* 1949, Mar., v. 8, No. 1, 80–84, 1 fig.

The author and his colleagues [this *Bulletin*, 1949, v. 46, 119] produced evidence to show that there was a synergism between chlorguanide [proguanil] and sulphadiazine when used to treat *P. gallinaceum* infections of chickens. He has now investigated the possibility that a chlorguanide-resistant strain of this organism might show increased sensitivity to sulphadiazine. Such a strain was therefore prepared by treatment of chicks with 0·03 mgm. of chlorguanide hydrochloride per gm. of body weight once or twice during each passage, and resistance was 16 to 32-fold from the 18th to 41st passage. During earlier passages and up to the 41st the resistant strain was at its maximum 8 times more sensitive to sulphadiazine than the normal. In later passages when chlorguanide treatment was discontinued, hypersensitivity to sulphadiazine persisted. As shown by others, the resistant strain was normally sensitive to quinine, chloroquine and pamaquin (plasmoquine). The author suggests that his findings indicate an attack by the two drugs in question on different enzyme systems in the parasite. They are, however, at variance with the findings of BISHOP and MCCONNACHIE [this *Bulletin*, 1949, v. 46, 119] who produced resistance to sulphadiazine in *P. gallinaceum* after 12 months' treatment, which was unaffected by mosquito passage and involved the simultaneous production of resistance to paludrine [proguanil]. A paludrine-resistant strain after months of contact with the drug was also resistant to sulphadiazine. These conflicting results of the different authors require further investigation. *J. D. Fulton*

MCGHEE, R. B. **Infection of Mammalian Erythrocytes by the Avian Malaria Parasite,** *Plasmodium lophurae*. *Proc. Soc. Exper. Biol. & Med.* 1949, May, v. 71, No. 1, 92–3, 1 fig.

Heavy infections of *Plasmodium lophurae* can be obtained in chicken embryos also and the author refers to an investigation at present under publication. Mammalian erythrocytes will survive for varying periods if introduced intravenously into the chicken embryo. Dog, rabbit and guineapig cells do not adapt themselves well to transfer, but human and murine erythrocytes retain their morphology for considerable periods. Accordingly, the author infected 10-day chick embryos with *P. lophurae* (24th passage strain in embryos) and two days later inoculated them intravenously with 0·2 cc. of twice washed erythrocytes. The parasites only

rarely invaded human corpuscles but mice cells were readily parasitized (up to 0·1 per cent.). The embryos usually showed a proportion of 1 : 2 mammalian to avian erythrocytes. The foreign cells were invaded after 12 hours, pre-segmenting forms were seen after 32 hours and mature schizonts in 36 hours. Band forms occurred, the pigment was in small golden-brown spheres and 5–11 merozoites in a rosette were produced. The mouse cells became enlarged but not stippled. No gametocytes were found.

In vitro, whole mouse blood plus infected chick embryo blood cultured by Trager's method [this *Bulletin*, 1947, v. 44, 1046] showed a similar invasion of the mouse erythrocytes by the parasite.

[This paper appears to the reviewer to be of considerable importance and the results indicate that the method will help in the solution of a number of problems in immunity, in the obscure subject of gametocyte production and in the general relationships of the different species of *Plasmodium*. Many queries suggest themselves : could the infection continue if the blood were returned to mice, would continued passage under these conditions increase the susceptibility of the mouse corpuscles to infection and, finally, how would other parasites react to such changes in environment ?] *P. C. C. Garnham*

BLACKWATER FEVER

Raoult, A., Auffret, C., Tanguy, F. & Martin, M. L'acide ascorbique dans le traitement de la fièvre bilieuse hémoglobinurique. [**Ascorbic Acid in the Treatment of Blackwater Fever.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 161–6.

Extremely low blood ascorbic acid levels were found in cases of acute and chronic malaria. In the blood of six out of nine patients who developed blackwater fever only immeasurable traces could be detected. Accordingly, persons suffering from this disease thereafter were given large doses of vitamin C, 200 mgm. intravenously every four hours, in addition to their other treatment, with good clinical results.

It is known that fever causes increased utilization of ascorbic acid and lowered blood and tissue levels, and, further, that ascorbic acid is a factor in maintaining corpuscular integrity by inhibiting liberation of histamine and by its antagonistic action to hyaluronidase. The authors consider that a critical lowering of ascorbic acid levels may be a major factor in precipitating the onset of blackwater fever and that this catastrophe might be prevented by administering large doses of vitamin C to all patients with malaria.

Dean A. Smith

TRYPANOSOMIASIS

Congo Belge. Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge. Rapport sur l'Activité durant les Années 1946 et 1947 [de Brauwere, P.]. Maladie du Sommeil. [**Sleeping Sickness.**] pp. 50–67, 1 diagram & 2 maps.

For the preceding Foréami Report, covering the years 1939 to 1945, see this *Bulletin*, 1948, v. 45, 816. The present Report as a whole is reviewed separately [*ibid.*, 1949, v. 46, 785]. In 1946 and 1947 the measures against sleeping sickness continued to consist mainly of mass treatment and

chemoprophylaxis, with only slight attention to entomological control. The situation continues to improve, as shown by a further decrease in the Index of New Cases. In the Kwango Sector, now the main scene of operations, the index was 0·47 per cent. (2,862 new cases) in 1940 and it had fallen to 0·16 per cent. (974 new cases) by 1947. Chief credit for the improvement is accorded to the procedure of mass-prophylaxis, which is being increasingly carried out with pentamidine or propamidine replacing suramin for this purpose.

Arsenic-resistant infection has been a considerable problem, and the Report refers to the discordance between the contention that arsenic-resistant strains are characterized by feeble infectivity and transmissibility [VAN HOOF, this *Bulletin*, 1947, v. 44, 1048] and the field observation that when a strain becomes resistant it also seems to cause a flare-up of the endemo-epidemic situation. However, the rising incidence of arsenic-resistant cases seems now to have been stemmed by the increasing use of mass prophylaxis.

In the 12 years up to December 31st, 1947, the Foréami has treated, in the Kwango Sector, 57,137 sleeping sickness cases, of whom 87·2 per cent. were cured, 2·1 per cent. are still under treatment, 4·1 per cent. have disappeared, and only 5·4 per cent. have died. Detailed statistics are given for each sub-sector. *E. M. Lourie*

WILLCOCKS, R. G. **Determination of Proteins in Cerebro-Spinal Fluid.** [Correspondence.] *Nature.* 1949, Feb. 26, 329–30.

In view of the need felt by many medical men concerned with sleeping sickness for improved methods of estimating the protein content of cerebrospinal fluid, the author, working in the Government Chemical Laboratory in Accra, has elaborated a method depending on the xanthoproteic reaction. This obviates some of the objections inherent in existing methods which depend on the estimation of opalescence or volume of precipitate.

The details cannot be usefully presented in the form of an abstract, and the original, very concise, paper should be consulted by those interested. [The method seems rather too complicated to be likely to find favour with field officers who have no taste, time or facilities, for refined chemical procedures.] *E. M. Lourie*

GASQ, M. Glycémie et glycorachie dans la période d'état de la trypanosomiase humaine. [**Glucose Content of the Blood and Cerebrospinal Fluid in Sleeping Sickness.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 93–7.

Glucose estimations were made on the blood and cerebrospinal fluid in 71 poorly nourished patients in both stages of sleeping sickness. Specimens were taken 12 hours after the last meal. Control observations were made on 48 uninfected subjects. No significant difference was found between the infected and the uninfected groups in respect either of the blood or of the cerebrospinal fluid. *E. M. Lourie*

TOWN, B. W., WILLS, E. D. & WORMALL, A. **Action of Suramin on Enzymes.** *Nature.* 1949, May 7, 735–6. [11 refs.]

The carbohydrate and oxidative metabolism of trypanosomes occurs at a relatively very high rate. One theory of the mode of chemotherapeutic action of suramin (antrypol, Bayer 205) is that it combines with or otherwise inhibits enzymes in the trypanosome which are necessary for this vigorous metabolism. The authors are, therefore, studying the action of suramin on various enzyme

systems, including those of the trypanosome. So far their attention has been confined mainly to the yeast enzymes concerned with carbohydrate metabolism and some other enzymes selected for special reasons.

It had previously been found that suramin is toxic to fumarase but not to urease [this *Bulletin*, 1932, v. 29, 295]. The authors confirm that urease is not affected at *p*H 7·5, but they find that marked inhibition occurs at *p*H 5. This is perhaps related to the presence of a urea structure in suramin, and it may depend on competitive inhibition though it may alternatively be due to the compound's sulphonic acid groups. The inhibition is evidently of a specific nature, since it is not exercised against enzymes in general when tested at *p*H 5 as might have been expected in view of the fact that suramin combines with a variety of proteins at that hydrogen ion concentration.

Trypsin has also been found to be much more sensitive to suramin than was previously reported. This may be due to the similarity between the urea linkage of suramin and the peptide linkage of proteins.

The fermentation of glucose by yeast juice is inhibited by suramin in concentrations considerably below those that might be present in the blood after dosages such as are used in clinical practice. *E. M. Lourie*

SCHLEYER, W. L. & SCHNITZER, R. J. **The Inhibition of the Anti-Trypanosomal Activity of Arsenoso Compounds and Acridines by Esters and Amides of Organic Acids.** *J. Immunology.* 1948, Oct., v. 60, No. 2, 265–76. [18 refs.]

This interesting paper describes a new category of interference effect against the anti-trypanosomal activity of arsenicals and acridines. Some of the categories of interference with arsenicals already well established are those due to the following :—

(i) Parafuchsin [BROWNING and GULBRANSEN, this *Bulletin*, 1922, v. 19, 882].

(ii) Thiol compounds [VOEGTLIN, DYER and LEONARD, this *Bulletin*, 1924, v. 21, 414], development of which led to the discovery of BAL as an antidote for arsenical poisoning by the team led by PETERS during the recent war.

(iii) *p*-aminobenzoic acid, in relation to *p*-arsenosophenylbutyric acid [WILLIAMSON and LOURIE, this *Bulletin*, 1947, v. 44, 48].

(iv) Melamine, in relation to melaminyl arsenicals [WILLIAMSON and LOURIE, this *Bulletin*, 1948, v. 45, 413].

The new interference phenomenon has been demonstrated both *in vitro* and *in vivo*. The two arsenicals mainly studied were both phenylarsenoxides, namely mapharsen and N-(*p*-arenosobenzyl)-glycineamide hydrochloride ; the acridine was acriflavine. The interference was exhibited by simple esters and amides of substituted benzoic acids (*e.g.* methyl-*p*-hydroxybenzoate and *p*-hydroxybenzamide), and by corresponding nicotinic acid derivatives. The acids themselves, tested as sodium salts, were inactive. When the newly discovered antagonists were used together with thiol substances, an additive or synergistic inhibitory effect was observed. A similar synergistic inhibition was noted, in respect of acridine but not of arsenical activity, when the new compounds were used in conjunction with yeast nucleic acid, which is known to be an inhibitor for the antibacterial effects of acridines.

Arsonic acids and arsenobenzenes were not antagonized by the new substances, nor were trivalent or pentavalent antimonials.

A table shows various points of difference between the features of inhibition exercised by some of the known types of interfering agent. For example, the new compounds do not affect toxicity of the arsenicals for the host, as do thiol compounds ; again, inhibition by the new compounds is demonstrable both *in vitro* and *in vivo*, while inhibition by parafuchsin is said to be demonstrable only *in vivo*. The authors accordingly infer that essentially

different mechanisms of inhibitory effect are involved. They have shown that methyl *p*-hydroxybenzoate not only inhibits the antagonistic effect of arsenoso compounds on isolated enzyme systems of *Bact. coli*, but may even exercise a stimulant effect on some of these enzymes. This suggests a possible basis for the mechanism of inhibitory effect of the substances concerned.

E. M. Lourie

SCHOENBACH, E. B. & GREENSPAN, E. M. **The Pharmacology, Mode of Action and Therapeutic Potentialities of Stilbamidine, Pentamidine, Propamidine and other Aromatic Diamidines—a Review.** *Medicine.* 1948, Sept., v. 27, No. 3, 327–77. [195 refs.]

This is a detailed and comprehensive survey of the development and present status of the diamidines as therapeutic agents. They are, of course, best known as remedies for protozoal infections, and their use in this connexion has been adequately reviewed in this *Bulletin* as the work has proceeded. Those who are not familiar with the progress of research on the diamidines in fields other than that of tropical medicine may be interested to know that there have been several surprising and significant developments in these other fields. Propamidine might have become very widely used as a wound disinfectant, if not for the discovery of sulphonamides and penicillin. More striking is the fact that diamidines have some degree of tumour-inhibiting activity. There is evidence that they combine with and inactivate specific nucleic acids or nucleoproteins, thus preventing the growth of certain tumour cells as studied in laboratory animals and in tissue cultures. This property apparently also underlies the fact that stilbamidine has a remarkably ameliorative, though not a curative, effect on multiple myelomatosis in man. Of more direct interest to tropical workers is the finding that propamidine exercises an inhibitory effect against a limited range of fungi *in vitro* [*Bulletin of Hygiene*, 1945, v. 20, 760]. The treatment of fungus diseases by diamidines might accordingly be worth investigating.

[The authors state that the early work of LOURIE and YORKE [this *Bulletin*, 1940, v. 37, 404] established the aromatic diamidines as potentially active agents against infections with African trypanosomes such as *T. rhodesiense* and *T. gambiense*. It might here be mentioned, though, that all the published work up to the present on field trials, as distinct from trials in laboratory animals, with the aromatic diamidines against the trypanosomes of man have been carried out against *T. gambiense* infections. It is a curious gap in the study of these compounds that no report has yet appeared on their action against naturally occurring *T. rhodesiense* infections.] *E. M. Lourie*

FULTON, J. D. & GOODWIN, T. W. **Hydrolytic Changes in Solutions of Stilbamidine.** *J. Pharm. & Pharmacol.* London. 1949, Jan., v. 1, No. 1, 11–16, 6 figs. on 1 pl. [13 refs.]

Working in the Sudan, HENRY [this *Bulletin*, 1944, v. 41, 196] found that among the changes undergone by stilbamidine solutions in diffuse daylight, there is hydrolysis of the amidine groups to the corresponding mono- and di-amides. In fact he isolated and identified 4-carbamyl-4′-amidinostilbene from such solutions [HENRY, *J. Chem. Soc.*, 1945, 870]. In England, FULTON [this *Bulletin*, 1948, v. 45, 508] found that the only product formed by exposure of stilbamidine solutions to light was 1 : 2 : 3 : 4-tetra-(4′-amidinophenyl) *cyclo*butane.

In 1947, Drs. Henry and Kirk sent the authors some bottles of stilbamidine hydrochloride solution prepared in the Sudan and kept since 1941 and 1942 in the dark or in diffuse sunlight. The solutions contained two types of crystalline deposit, one of which the authors have confirmed as 4-carbamyl-4′-amidino-stilbene and the other they have identified as 4 : 4′-dicarbamyl-stilbene.

Since deposits had never been observed in stilbamidine solutions kept for more than a year at room temperature in England, the authors prepared further solutions which they then subjected to various conditions of light and temperature over a period of 6 months. Under certain conditions deposits appeared, consisting of mono- and diamides identical with the products formed in the Sudan. Temperature is apparently important, for the monoamide (though only traces of diamide) were obtained by keeping solutions at 37°C. for 6 to 17 weeks, while no amides were formed at laboratory temperatures. Occasional exposure to electric light also increased the yield considerably, as compared with solutions kept in complete darkness. Good yields of both amides were readily obtained by autoclaving for several hours at 1 to 2 atmospheres pressure.

Tests showed the monoamide to be more toxic than stilbamidine and inactive against *T. rhodesiense* and *T. congolense* infections in mice. Similar tests with the diamide were not possible because of its relative insolubility. Studies of fluorescence on ultra-violet illumination showed that stilbamidine is selectively concentrated at the blepharoplast and at a point near the anterior end of both *T. rhodesiense* and *T. congolense*, while the monoamide is diffusely distributed throughout the bodies of these trypanosomes.

Autoclaving solutions of stilbamidine for only 20 minutes at 5 lb. pressure, the method used by OASTLER and FIDLER [this *Bulletin*, 1946, v. 43, 1029] did not produce any demonstrable chemical change and did not increase the toxicity of the solutions for mice. It is therefore suggested that the lesions described by these workers in dogs treated with such solutions were due to unchanged stilbamidine. *E. M. Lourie*

NODENOT, L. Note sur une infection accidentelle avec une souche de *Trypanosoma gambiense*. [**An Accidental** *T. gambiense* **Infection.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 1/2, 16–18.

The infection was accidentally contracted in the laboratory in Paris, and is evidently the one mentioned by LAUNOY [this *Bulletin*, 1949, v. 46, 337]. There was an incubation period of 10 days, followed by regular intermittent bi-quotidian fever, with severe headache and general symptoms. Parasites were numerous in the blood, and the spleen was enlarged. Lymph glands were not palpable and the cerebrospinal fluid was normal. Lomidine was given intramuscularly, 0·2 gm. (*i.e.*, 3·25 mgm. per kgm.) daily for 5 days. Trypanosomes disappeared the day after the first dose, and the original symptoms and signs rapidly cleared up. However, the patient began to complain of pain in the buttock, where a tender induration could be felt.

There was a rest-period of 8 days, and another 5-day course of lomidine treatment was then started. After the first injection the patient complained of a bitter taste in the mouth, a feeling of constriction in the throat, recrudescence of the pain in the buttock, difficulty in walking, and weakness. The symptoms became worse during treatment, which was accordingly stopped after the third injection. It took 6 weeks to recover from these symptoms, which the author ascribes to saturation of the body with the drug, and which were reminiscent of those described by SICÉ in another accidental laboratory infection treated with pentamidine [see this *Bulletin*, 1948, v. 45, 876]. *E. M. Lourie*

BEAUDIMENT, R., BROCHEN, L. & PEUZIAT, Y. Note sur l'action curative du diamidino-diphénoxypentane administré par voie orale, dans la trypanosomiase humaine africaine. [**Treatment of Sleeping Sickness by Lomidine administered Orally.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 1/2, 18–22.

Twenty-one cases of *T. gambiense* sleeping sickness, early and late, were treated orally by lomidine (dimethanesulphonate of pentamidine base). The drug was given either in a single dose or fractionated every day for 5 days. The daily dose for most patients was 20 to 30 mgm. per kgm. A total for the 5 days of 120 mgm. per kgm. was perfectly tolerated by some, but others who received 73 and 114 mgm. per kgm. suffered from diarrhoea and vomiting.

In 60 per cent. of cases the trypanosomes had disappeared from the blood and cerebrospinal fluid within 24 hours of a first dose of 20 to 30 mgm. per kgm. ; and in all cases, early and late, they had disappeared by the end of treatment-courses varying from 114 to 150 mgm. per kgm. for the period of 5 days.

Of 9 first-stage patients there were 2 relapses within a fortnight. The other 7 have been under observation for periods of 1 to 5 months. No information is yet available on the fate of the second-stage cases.

The authors admit that the oral route appears to give therapeutic results inferior to those obtained by injection, but they are undeterred from exploring the potentialities of oral administration for prophylaxis. " Only an experiment conducted on a vast scale will permit the fixing of optimal prophylactic dosages. We propose to carry out such an experiment." *E. M. Lourie*

GASQ, M. Action de la Lomidine (2512 R.P.) sur la glycémie des trypanosomés en 1re et 2me périodes. (Premiers résultats.) [**Action of Lomidine on the Blood Sugar in Sleeping Sickness.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 99–105, 1 folding chart.

Blood sugar estimations were made on 8 patients undergoing treatment by lomidine (dimethanesulphonate of pentamidine base) for the early or late stages of sleeping sickness. Treatment was by 3 mgm. per kgm. intramuscularly every alternate day for 5 injections. The blood was examined not less than 12 hours since the last meal, specimens being taken immediately before an injection, and then at intervals of 10 minutes for one hour.

Results were similar in the two stages of infection. There was an increase from an average of about 93 mgm. per 100 cc. to a peak of 106 mgm. in 20 minutes. There was then a drop to about 80 mgm. at 30 minutes, followed by a gradual rise to the original level at the end of the observation period of one hour. *E. M. Lourie*

FRIEDHEIM, E. A. H., VOGEL, H. J. & BERMAN, Rose L. Un composé organique stibié curatif et prophylactique dans la trypanosomiase expérimentale. [**An Organic Antimony Compound with Curative and Prophylactic Activity in Experimental Trypanosomiasis.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 85–8.

This is substantially a French translation of an earlier paper by FRIEDHEIM and BERMAN [this *Bulletin*, 1946, v. 43, 1124], with a few omissions and with additional data showing that the prophylactic action of the compound in question (MSb) is superior to that of suramin (moranyl) for *T. equiperdum* infections of mice. One-fiftieth of the maximum tolerated dose of MSb intraperitoneally protected all of five mice inoculated 68 days later, but a comparable dose of suramin protected none of five mice tested on the 61st day.

E. M. Lourie

LE ROUZIC, J. & LAPEYSSONNIE, L. Les médicaments nouveaux dans la trypanosomiase. [**The New Drugs for Sleeping Sickness.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 7–22.

The author reviews French West African experience with FRIEDHEIM's melaminyl compounds, the diamidines, and EAGLE's " 70A ".

Melarsen.—[See FRIEDHEIM, this *Bulletin*, 1941, v. 38, 634 ; NODENOT, this *Bulletin*, 1949, v. 46, 238.] Of 22 late cases treated at Bobo with samples received since 1946, the cerebrospinal fluid was restored to normal in 8 and improved in 6. Unlike tryparsamide, which either renders the cerebrospinal fluid normal " immediately " or leaves it unchanged, melarsen brings it back to normal by slow stages over a period of some months. There were no instances of damage to the optic nerve. Melarsen is said to have the further advantage that it acts on trypanosomes both in the lymphatico-blood system and in the central nervous system ; French workers hold that tryparsamide acts only in the latter situation.

Melarsen oxide and *Mel B* (*or Melarsen B.A.L.*).—[See FRIEDHEIM, this *Bulletin*, 1949, v. 46, 711.] These compounds are said to have the same advantages as melarsen, with the additional advantage that they can be given in a much shorter course of treatment. The author appears to place greater faith in Mel B than in Melarsen oxide. Success is claimed in 50 per cent. of an unspecified number of second stage cases.

MSb V.—[See FRIEDHEIM and BERMAN, this *Bulletin*, 1946, v. 43, 1124, and FRIEDHEIM, VOGEL and BERMAN, above.] All the field observations on this compound till now have been made by Dr. Friedheim himself. For treatment, as distinct from prophylaxis, it has been given either alone or in combined courses with the following :—

MSb III and *MSb B*, trivalent variants of *MSb V.*—These three compounds are active against early cases, but they have an inconstant and superficial action on second stage cases.

Diamidines.—The aromatic diamidines have been curative in 90 per cent. of early cases, but are undependable when there is even a slight alteration in the cerebrospinal fluid. A directive was accordingly issued for all first stage cases in French West Africa and in Togo to be treated by pentamidine (5 injections of 3 mgm. per kgm.) which is regarded as rather more effective than propamidine. Pentamidine will, however, gradually be replaced by " lomidine ", the dimethanesulphonate of pentamidine base. Among 1,011 first stage cases treated by pentamidine there have so far been 93·7 per cent. cures, without any toxic complications. There were only 2 cases (0·02 per cent.) of chemo-resistance, and even these were not fully substantiated.

70A or p-arsenosophenylbutyric acid.—[See EAGLE, this *Bulletin*, 1946, v. 43, 1017.] Although this compound is ineffective in second stage cases when given alone, the results have been " brilliant ", with 75 per cent. successes, when it was given in combination with tryparsamide. The compound is, therefore, said to be " not without interest ". [CECCALDI *et al.*, this *Bulletin*, 1948, v. 45, 771 found combined treatment with 70A and tryparsamide to give results inferior to those obtained with established forms of treatment.]

E. M. Lourie

WILSON, S. G. **Drug-Resistance shown by Trypanosomes following " Antrycide " Treatment.** [Correspondence.] *Nature.* 1949, June 4, 873–4.

At Entebbe the soluble salt of " Antrycide ", in doses of 3–5 mgm. per kilo, cured *T. simiae* infections in pigs. One pig relapsed after 2 mgm. per kilo of the relatively insoluble chloride ; a second treatment with 5 mgm. per kilo of the

soluble salt, the sulphate [presumably methylsulphate], then failed to cure, and the relapse strain was therefore considered to have become resistant.

Ten cattle were dosed with 2 gm. each of " Antrycide " sulphate, and were then exposed to infection in a *G. pallidipes* area. Only one was still alive six months later, and a strain of *T. congolense* passaged from this animal into a calf resisted treatment with 5 mgm. per kilo of the sulphate. Two of six mice infected with this strain relapsed after treatment with 10 mgm. per kilo of the sulphate. A field strain collected in the same area from an untreated ox was cured by 0·5 mgm. per kilo.

Some animals re-infected several months after treatment with antrycide and re-treated with curative doses have developed cryptic but nevertheless fatal infections.

There is some evidence that *T. vivax* likewise quickly develops resistance to antrycide, and there is evidence also that *T. congolense* which develops resistance to antrycide as a result of treatment with this compound becomes resistant at the same time to dimidium bromide.

Doses in excess of 10 mgm. per kilo [no doubt of the soluble salt] may be rapidly toxic, the animal dying 2 to 6 hours after treatment ; in other cases gastro-enteritis develops 2 days after treatment and death occurs between the sixth and twelfth days. *E. M. Lourie*

British Med. J. 1949, June 11, 1046–7. **Control of Trypanosomiasis. Insecticides and Antrycide.**

A general article based on an address by Dr. D. G. Davey on the use of antrycide against trypanosomiasis in animals, particularly cattle, in Africa. Although antrycide is a very promising drug and has been shown to give protection to cattle for at least 4–6 months, the possibility of naturally, or artificially induced, resistant strains of trypanosomes being encountered had to be borne in mind. Only further trials and observations would show what contribution to the development of Africa could be expected from antrycide.

[See this *Bulletin*, 1949, v. 46, 338.] *D. S. Bertram*

Launoy, L. & Jeanpierre, C. Nouveaux documents sur la prophylaxie chimique de l'infection à *T. equiperdum* du rat blanc, par ingestion de diamidino-diphénoxypentane. [**New Observations on the Chemoprophylaxis of *Trypanosoma equiperdum* Infection in the White Rat by Ingestion of Diamidino-diphenoxypentane.**] *C. R. Soc. Biol.* 1949, Mar., v. 143, Nos. 5/6, 328–9.

Rubin, B. A. **An *in vitro* Assay for Trypanocidal Activity.** *Yale J. Biol. & Med.* 1948, Mar., v. 20, No. 4, 381–93.

The classical method of Yorke, Adams and Murgatroyd [this *Bulletin*, 1930, v. 27, 237] for keeping pathogenic trypanosomes alive at 37°C. for 24 hours depends on suspending these organisms in a concentration not above 1,000 per cmm. in a medium composed of inactivated sheep or rabbit serum diluted with Ringer solution containing 0·2 per cent. glucose. It is on this method that the author bases his own technique, which he describes in minute detail, for *in vitro* assay of compounds against *T. equiperdum*. The medium he uses is pooled human serum centrifuged at 2,000 r.p.m. for 2 hours and diluted with twice its volume of special Ringer glucose solution. The medium is then Seitz-filtered and inactivated at 62–63°C. for half an hour. The final *p*H is 8·3 to 8·5. Heavily infected mouse blood is then mixed with an equal volume of citrated Ringer solution and 0·05 cc. added to each 10 cc. of medium so that there should be 500 to 1,500 trypanosomes, and 10 to 20 times that

number of red blood cells, per cmm. Drug solutions are added in amounts of 0·1 cc. in distilled water to 0·4 cc. of infected medium. After 18 to 20 hours at 37°C. the specimens are examined for trypanosomes and haemolysis.

The Ringer glucose solution recommended by YORKE contained 0·9 per cent. sodium chloride. The author finds it better to use 0·75 per cent., and the final concentration of sodium chloride is even less after the solutions of drug in distilled water have been added.

Some batches of medium completely failed to support trypanosomes, and this the author attributes to the possibility that one of the donors from whom the pooled serum was obtained might recently have received an injection of an arsenical. *E. M. Lourie*

RUBIN, B. A. **The Trypanocidal Effect of Antibiotic Lactones and of their Analogs.** *Yale J. Biol. & Med.* 1948, Jan., v. 20, No. 3, 233–72. [38 refs.]

The method described by the author [above], was used in order to investigate the trypanocidal potentialities of antibiotic lactones and their analogues. Such substances are widely distributed in nature, particularly in lichens, moulds, and higher plants. They occur in various natural dyes, in vitamin E, in the haemorrhagic principle of clover, in fish poisons, in insecticides, in numerous alkaloids, and in the digitalis glycosides. Furane analogues of lactones occur in large amounts in corn-cobs, oat-hulls, and other plant substances ; and one of these compounds, " Furacin " has already been shown to have some action on trypanosome infections [DODD, this *Bulletin*, 1948, v. 45, 52]. Pyrroles, nitrogen analogues of the furanes, are also widely distributed in nature, being best known in porphyrin pigments and in various animal and plant dyes.

Altogether 44 compounds were tested. " Furacin " was the most promising. Delta lactones were more active than gamma lactone analogues, the three lactones with highest *in vivo* activity being 2-pentene-1,4-olid, penicillic, and coumalinic acids. There was no correlation between *in vivo* and *in vitro* effects. Thus clavicin was one of the most highly trypanocidal substances *in vitro*, but it was too toxic for any *in vivo* property to come into effect. This substance has no surface tension reducing power at room temperature, and yet it is trypanocidal in a dilution of 1 in 1,000,000 at that temperature, a finding which the author says is at variance with theories which require some surface effect to occur before a drug can exercise its biological action. In other instances there was high surface activity with neither trypanocidal nor haemolytic effect.

Beside " Furacin " two other furanes showed some action *in vivo*, furfural and furfuryl alcohol. Hydrogenated furanes were inactive.

All nitrogen analogues tested were toxic and inactive *in vivo*.

Most of the compounds were also tested against *Shigella dysenteriae* and *Staphyloccus aureus*, but no quantitative relationship was found between antibacterial and trypanocidal activities. *E. M. Lourie*

VILAIN, P. De la répartition géographique des glossines en A.O.F. [**The Geographical Distribution of Tsetse Flies in French West Africa.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 107–16.

Since the days of Roubaud and Bouet, some forty years ago, little that is new has been recorded about *Glossina* in French West Africa. The author has carried out field work in the Upper Volta. He has also received very many specimens collected by the medical staff in many districts. Of a total of 120,000 specimens, over 95 per cent. were *G. palpalis*, *tachinoides* or *morsitans*. Six other species were represented in small numbers.

The paper reports geographical distribution, but in a rather general manner, and without adding much precision to what is already known. We feel that in assessing the commonness of an insect the author relies too much on the number of specimens sent in. Some species may well be overlooked unless special methods of collecting are employed. *P. A. Buxton*

UGANDA PROTECTORATE. **Annual Report of the Tsetse Control Department for the Year ended 31st December, 1947** [SLAUGHTER, B. I., Acting Director of Tsetse Control]. 18 pp. 1948. Entebbe: Govt. Printer. [Shs. 1/50.]

LE ROUZIC. La prophylaxie agronomique. Un moyen de lutte pour l'assainissement des régions infestées. [**Tsetse Control by Agricultural Methods.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 117–22.

An autonomous sleeping sickness service was initiated in French West Africa in 1939. The present paper gives a general account of its work.

In most respects the methods in use are those which are generally familiar. We notice that the French put much emphasis on "*prophylaxie agronomique,*" which is equivalent to the cultivation of the area which has been cleared, and its occupation by human beings. In making a waterside clearing close to an infected village, they recommend a clearing 50 metres wide and 700 long, against *G. palpalis*: rather smaller clearings are said to be sufficient against *G. tachinoides*. British experience would lead one to expect that such clearings are not sufficiently long to give complete protection from either of these insects. The French view is, we think, that this rather short clearing combined with diagnosis and treatment of human cases gives satisfactory results, at least in savannah country. In forest where no doubt clearing would be very expensive both in primary cost and annual maintenance, the author says that drugs alone do not overcome sleeping sickness; the number of new cases in successive years appears to demonstrate this.

The author attaches much importance to the sacred groves which often occur on the edge of a village. The local people cannot in any way interfere with these places, which form breeding places of *Glossina* in close contact with man. These places have been very numerous in the Upper Volta and their destruction is a most important measure in the reduction of fly and the control of sleeping sickness. We note that the French make much use of the labour of individuals in good health who are under treatment or have been recently treated for trypanosome infections. They can on occasion also obtain voluntary labour from villages.

The paper contains statistics for a number of years, showing the area cleared and planted, and the number of new cases of trypanosomiasis for different regions of French West Africa. *P. A. Buxton*

WHITESIDE, E. F. **An Experiment in Control of Tsetse with DDT-treated Oxen.** *Bull. Entom. Res.* 1949, May, v. 40, Pt. 1, 123–34, 2 figs. [17 refs.]

The object of this experiment was to determine the feasibility of exterminating tsetse flies by introducing a large number of cattle treated with DDT into their habitat. An area of thorn bush about 5 square miles in Tanganyika was chosen for the test. There was evidence that this territory was relatively isolated from external sources of tsetse flies owing to 1½ miles of clearing all round. The cattle were grazed in herds of 10 (Phase I) or 5 (Phase II) at the rate of 68 to the square mile. They were thus about 6 times as numerous as large game but less common than small game.

The DDT treatment was by a solution of 9 per cent. DDT and 9 per cent. resin in groundnut oil, applied all over the body (except the head) to give about 10 gm. DDT per animal (450 mgm. per sq. ft.). This treatment was applied weekly at first and later twice a week. Two months of this regular treatment did not harm the cattle.

The tsetse fly populations were assessed by 48 random catches per week. (Two boys with a black cloth moving at random for two hours constitutes a "catch.") The results of the experiment were estimated by two arithmetical methods described in detail; one depends on changes in numbers on the test area, the other depends on relation to fly catches in an external control. A mean of the two estimates was considered most reliable.

According to the observed reductions, the mean kill of flies was about 70 per cent. during Phase I and 95 per cent. in Phase II. At the rate of progress observed, it was calculated that extermination of tsetse flies would take 22 months with herds of 10 cattle and about 9 months with herds of 5. Further splitting of the cattle would require too many herdsmen.

The slow progress of the reduction is due to tsetse flies feeding on animals other than the treated cattle. It would not be possible greatly to increase numbers of cattle because they were near the limit which can be supported on this type of country.

J. R. Busvine

See also p. 984, Lourenço Marques, Moçambique: **Missão de combate as tripanossomíases. Relatório anual de 1947.**

Faust, E. C. **The Etiologic Agent of Chagas' Disease in the United States.** *Bol. Oficina Sanitaria Panamericana.* 1949, May, v. 28, No. 5, 455–61. [24 refs.]

This paper reviews the information available on the occurrence of triatomid bugs and mammals naturally infected with *Trypanosoma cruzi* in the United States of America. A list is also given of the bugs and mammals successfully infected experimentally. The data are conveniently set out in tables showing the names of the insects and the mammals, their geographical origin, and the references to the original papers from which the information has been extracted.

There is apparently no substantial published evidence that Chagas's disease occurs in man in the United States despite the considerable evidence of its occurrence as a disease of lower mammals. Seven mammals and seven species and two subspecies of triatomid bug have been found naturally infected.

It is concluded that the apparent absence of human infections in the presence of this animal reservoir cannot yet be adequately explained. Steps should, it is suggested, be taken meanwhile to control the bugs in infested premises and to carry on further investigations on the habits of the bugs.

D. S. Bertram

Pifano, F. Nouvelle trypanosomiase humaine de la région néotropicale produite par le *Trypanosoma rangeli* Tejera, 1920. [**A New Form of Human Trypanosomiasis of Neotropical Regions, produced by** *Trypanosoma rangeli* **Tejera 1920.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 11/12, 671–80, 3 figs.

This paper is, in large part, a recapitulation of work already published by Pifano and his colleagues on the occasion of the first successful direct cultivation of *Trypanosoma rangeli* from the peripheral blood [this *Bulletin*, 1948, v. 45, 1072]. Previous findings of *T. rangeli* in reduvid bugs or in human patients are discussed and the fact is noted that the authors have now

demonstrated that natural infections with *T. rangeli* are found in dogs as well as in man. In one dog the parasite was encountered in direct examination of the peripheral blood. Work on the parasite is in progress. A detailed description is given of the morphology of the parasite in the peripheral blood, in reduvid bugs and in cultures. It is considered that *T. rangeli* is now established as a parasite of man and the dog, and that in consequence, there must be considered to be two forms of trypanosomiasis in the New World, due to *T. cruzi* and *T. rangeli*. *H. E. Shortt*

FLOCH, H. & ABONNENC, E. Sur l'identification de *Trypanosoma conorrhini* (Donovan 1909); sa présence en Guyane française. [**The Identification of** *Tryponosoma conorrhini* (**Donovan 1909**) **and its Presence in French Guiana.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 5/6, 221–9, 4 figs. [18 refs.]

LEISHMANIASIS

BHASKARAN, K. **A Report of Two Cases of Kala Azar with Delirium as a Prominent Feature.** *Indian Med. Gaz.* 1949, Apr., v. 84, No. 4, 139–40.

TRINCÃO, C. Sindroma anémico do kala-azar. [**Anaemic Syndrome in Kala Azar.** 68 pp. [Numerous refs.] 1948. Lisbon.

This is a reprint of chapters III to VI of the author's fuller monograph [this *Bulletin*, 1949, v. 46, 127.]

i. SARROUY, C., ARNAUD-BATTANDIER, R. & CABANNES, R. Deux nouvelles observations de kala-azar infantile, traitées par le 2168 R.P. De la technique d'administration du 2168 R.P. [**Two more Cases of Infantile Kala Azar treated by 2168 R.P. The Technique of Treatment.**] *Algérie Méd.* 1947, Apr., No. 4, 333–9, 1 fig. & 4 charts.

ii. D'ESHOUGUES, J. R. & MESSERSCHMITT, J. Kala-azar de l'adulte guéri par une seule cure de 2168 R.P. [**Kala Azar in an Adult cured by a Single Course of 2168 R.P.**] *Ibid.* 1948, Mar., No. 3, 152–6, 2 figs.

iii. MÉDÉCINE TROP. Marseilles. 1948, July–Aug.–Sept.–Oct., v. 8, No. 4, 490–91. A propos du 2168 R.P. et de son dosage dans les urines. [**Concerning 2168 R.P. and its Estimation in the Urine.**]

i. For previous reports on the use of 2168 R.P. against kala azar see SARROUY *et al.*, [this *Bulletin*, 1947, v. 44, 55 and 807; and DURAND *et al.*, *ibid.*, 56.]

The present report concerns two infants, both very severely affected. The first patient was 13 months old, weighed 18·8 kgm., and had been ill for 5 months.

Anthiomaline, given on alternate days for 5 doses, was ineffective, but a 10-day course of 2168 R.P., 90 mgm. per kgm. daily intramuscularly, produced an immediate and striking improvement, maintained for the observation period of 3 months. The second case was in a child of 4 years, weighing 13 kgm., in wretched condition, suffering not only from kala-azar but also from pulmonary and peritoneal tuberculosis and an "intercurrent catarrhal jaundice." The drug was given in smaller doses and for a longer time than in the other case. There was some improvement, but parasites could still be seen at the end of treatment. He developed measles with an intense laryngitis and died.

The authors conclude by saying that a non-toxic antimonial like 2168 R.P. should be given in massive doses and in a short course of treatment.

ii. Most patients treated so far by 2168 R.P. have been children, but an adult case is here reported in considerable detail. The patient was 20 years old, weighing 58 kgm., and had been seriously ill for 8 months. He was treated by 100 mgm. per kgm. daily (except for the first two doses which were rather less), to a total of 76·5 gm. for the whole course. Results were excellent, over an observation period of two months, and the authors believe the patient to be cured. They write that all important references to previous use of this compound are given by R. SOHIER in the *Journal de Médecine de Lyon* for September 5th, 1947.

iii. A brief paper, over the initials G. F., declares that 2168 R.P. is rapidly and completely eliminated in the urine. Methods of urine estimation are described. *E. M. Lourie*

HAZARIKA, A. N. **Treatment of Kala-Azar with Pentamidine Isothionate. A Study of 55 Cases.** *Indian Med. Gaz.* 1949, Apr., v. 84, No. 4, 140–45.

A series of 55 Indian patients were treated for kala azar, with pentamidine isethionate [incorrectly referred to throughout as isothionate]. In each case the diagnosis was confirmed by the finding of leishmania by spleen puncture. Of the 55 patients 34 were antimony-resistant. The drug was given daily in a 10 per cent. solution, intravenously in 25 cases, intramuscularly in 28, and by both methods in the remaining two cases. The maximum daily dose was based on the weight of the patient; in 19 cases this was 1·0 mgm. per pound weight of patient and in 32 it was 1·5 mgm., in the other 4 it was just outside this range. To obviate toxic reactions, the initial doses were usually less than this maximum. Ten to twenty injections were given to each patient and the total relative dose (per 100 lb. weight of patient) ranged between 0·60 and 3·00 grammes.

The immediate reactions to intravenous injections were the vasomotor symptoms usually associated with the 4 : 4′diamidine drugs but they were not severe, except in one case and there were no late sequelae such as the neuropathies associated with stilbamidine. There were no immediate reactions after intramuscular injections. However, 4 patients developed oedema during or after treatment.

Three patients died and one absconded. The rest were clinically cured at the time of discharge—immediate cure rate 94·44 per cent. In a follow-up investigation, it was found that 6 months after the completion of the course 16 of the 42 followed up had relapsed, a relapse rate of 38·09 per cent.

The relapse rate among antimony-resistant cases was 33·33 and among the remainder 50·00 per cent. There was little difference in the relapse rate between those receiving 1·0 mgm. and those receiving 1·5 mgm. of the drug per pound weight; the figures were 46·6 per cent. and 34·78 per cent., respectively.

It is suggested that in view of the absence of toxic symptoms larger dosages might be employed. *L. E. Napier*

ADA, G. & FULTON, J. D. **Electrophoretic Studies on the Serum of Golden Hamsters infected with** *Leishmania donovani*. *Brit. J. Exper. Path.* 1948, Dec., v. 29, No. 6, 524–9.

During the first six weeks of *Leishmania donovani* infection in the golden hamster the serum pattern remains unchanged. There is then a marked decrease in the amount of albumin accompanied by an increase of α-globulin, the concentration of total protein remaining normal. There is a concurrent

lipaemia, involving phospholipids, cholesterol and fatty acids. These various serum changes were found to reach a maximum at the 9th week and then to persist, but with much diminution of the lipaemia, for the remainder of the observation period of 13 weeks.

When animals were treated with sodium stiboglucanate on the 65th day of infection and examined 12 days later (parasites then being too few to be detected) the serum protein pattern was found to have become practically normal. However, animals similarly treated, but killed 25 to 40 days later, showed the abnormal serum pattern characteristic of untreated infections; this reversion to the abnormal pattern was accompanied by a marked increase in the number of parasites. Since the drug treatment, although effective against the parasites, can hardly be thought to have influenced the amyloidosis, which is always a marked feature in the pathology of visceral leishmaniasis in the hamster, the authors conclude that the changes in the serum protein pattern and the lipaemia are due to the activity of the parasites rather than to the associated renal conditions.

The particular abnormality of the serum in human cases of kala azar responsible for the formal gel test does not occur in infected hamsters, since the test is always negative in these animals.

In specimens received from two patients suffering from kala azar in Malta it was confirmed that there is an increase in the γ-globulin component of the serum. *E. M. Lourie*

CAMPOS, J. A. A bogalita no tratamento da leishmaniose. [**" Bogalita " in the Treatment of [Cutaneous] Leishmaniasis.**] *Publicações Médicas.* São Paulo. 1948, Feb.–July, v. 19, No. 172, 7–13, 2 figs.

Bogalita or Rongalita C, is the commercial name of methanal [formaldehyde] sulphoxylate of sodium. It has been tried in leprosy and " all drugs active in leprosy have in their molecules one or more groups of SO_3Na or SO_2Na." A comparison of the following formulae will show that Bogalita contains the SO_2Na group of diasone and the SO_3Na group of promin.

$$CH_3CO—NH—SO_2—NH—COCH_3$$

Rodilone

$$OHCH_2—(CHOH)_4—\underset{\underset{SO_3Na}{|}}{CH}—NH—SO_2—NH—\underset{\underset{SO_3Na}{|}}{CH}—(CHOH)_4—CH_2OH$$

Promin

$$NaSO_2—CH_2—NH—SO_2—NH—CH_2—SO_2Na$$

Diasone

$$OH—\underset{\underset{SO_3Na}{|}}{CH_2}—H_2O—OH—CH_2—SO_2Na,\ 2H_2O$$

Bogalita

The author has tried this in three patients, giving it in 10 per cent. solution in distilled water, intravenously, over a period of two months, to a total of 150 gm., in doses of 5 gm. daily in two administrations. Early in the course the edges of the lesions become blanched, crusts form and scarring takes place. The blood picture, it is said, is unchanged. In the early stages there may be nausea and even vomiting, but if the injections are given slowly these symptoms soon disappear. Experimentally, 3 per cent. solution is bactericidal, 0·3 per cent. is bacteriostatic. [What organism is used for the test is not stated.] It is almost non-toxic; 1 gm. per kilo is tolerated by a rabbit. If it is found to be effectual *per os* it will be of value epidemiologically. *H. Harold Scott*

FEVERS OF THE TYPHUS GROUP

BOVARNICK, Marianna R. & SNYDER, J. C. **Respiration of Typhus Rickettsiae.** *J. Exper. Med.* 1949, June 1, v. 89, No. 6, 561–5. [12 refs.]

"Partially purified suspensions of typhus rickettsiae have been shown to exhibit metabolic activity as evidenced by consumption of oxygen and production of carbon dioxide in the presence of glutamate. Similar activity at a much lower rate occurs in the presence of pyruvate. The rate of oxygen uptake was directly proportional to the concentration of viable rickettsiae, as estimated by their toxicity for mice. Normal yolk sac suspensions prepared in the same manner showed only a very slight oxygen uptake under the same conditions. Glucose was not metabolized by the rickettsial suspensions."

TAMIYA, T., HAZATO, H., YAMAMOTO, T., IIDA, T., SHIMOJO, H., NISHIOKA, K., KAWAMURA, A., SUZUKI, K., ARAI, M., TSUKAMOTO, R. & SCHOBLE, Y. **Studies on the So-called X-Factor common to *Proteus OX19*, *Rickettsia prowazeki* and *Rickettsia mooseri*, especially on the relation of the Factor to Blood Group B Specific Substance.** *Japanese J. Exper. Med.* 1949, Mar. 1, v. 20, No. 1, 1–23, 2 figs. [35 refs.]

By an extensive series of serological and chemical experiments the authors have found reasons for believing that a specific heterogenetic antigen exists as a common partial antigen in *Proteus OX19*, *Rickettsia prowazeki*, and *R. mooseri*, and that the same factor exists in the blood of persons belonging to the B blood group and in the blood of rabbits and guineapigs.

The factor is regarded as existing in the Castañeda X-factor as a partial antigen, but it is not considered to be the substance that plays the chief part in the Weil-Felix reaction.

The authors believe that the factor is closely related to the substance to whose presence blood of the B group owes it specific properties.

The experiments and the discussion of the interpretation of their results do not lend themselves to the preparation of a summary. Workers on the antigens will wish to read the original paper. *John W. D. Megaw*

NEILL, G. A. W. **Typhus Fever in County Tyrone.** *Pub. Health.* 1949, June, v. 62, No. 9, 189–91.

Two boys, aged 7 and 16 years, living in a verminous hut in conditions of extreme neglect with their two brothers and grandmother, were attacked by louse-borne typhus fever in the months of June and July 1948. The diagnosis was confirmed—retrospectively in one of the cases—by Weil-Felix reactions at titres of 1–640 and 1–1,200.

The source of infection was strongly suspected to have been intimate contact with verminous nomadic "tinkers" who had recently arrived from Eire. An outbreak of typhus was known to have occurred in the adjoining County, Donegal, in 1940.

The author, who had just been appointed as the first whole-time Medical Officer of Health for Co. Tyrone, took energetic steps, including the isolation in hospital of the family; the destruction, with later replacement, of their bedding and clothing; the disinfestation with DDT of 278 persons and of 75 tents and vans belonging to nomadic gypsies or tinkers throughout the County. The nomads refused to co-operate except for submitting to dusting with DDT.

Children in all the schools within a radius of five miles were inspected, but no case of gross infestation with lice was detected.

No further cases of typhus have occurred up to the time of writing, nine months after the occurrence. *John W. D. Megaw*

RIS, H. & FOX, J. P. **The Cytology of Rickettsiae.** *J. Exper. Med.* 1949, June 1, v. 89, No. 6, 681–5, 1 text fig. & 12 figs. on 2 pls. [14 refs.]

The authors describe a series of studies in which highly specialized technical methods were employed, including the use of the phase-contrast and the electron microscope. Twelve excellent photographs, most of which were taken with these microscopes, show that *Rickettsia prowazeki* has a physical structure of the same type as most bacteria ; their " nuclear structures," or " chromatinic bodies " are sharply defined minute spheres, which are single in spherical forms of rickettsiae and vary in number from two to four in rod-shaped rickettsiae ; occasional dumb-bell forms occur, these are probably undergoing nuclear division.

By special cytochemical and staining methods the authors have found evidence to show that the nuclear structures, like those of bacteria, contain desoxyribonucleic acid as well as ribonucleic acid, whereas some previous workers have concluded that rickettsiae resemble viruses in containing only one type of nucleic acid. *John W. D. Megaw*

ZAHARIA, N. I. & DIMITRIU, A. Les réticulocytes au cours du typhus exanthématique. [**The Reticulocytes in Typhus Fever.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 104–21, 2 graphs.

The author gives a summary of modern views on the significance of changes observed in the number and type of reticulocytes during the progress of certain diseases.

In 25 typhus patients an irregularly progressive diminution occurred in the number of the reticulocytes after the 3rd or 4th day ; in some cases there was a total disappearance of the reticulocytes during the second week. There was a return to the normal number during convalescence. The diminution was most pronounced in the " old " reticulocytes so that the formula showed a deviation to the left, followed in the 3rd and 4th weeks by a slight deviation to the right.

The reticulocytopenia was regarded as being due to damage caused to the bone marrow by the typhus toxins. *John W. D. Megaw*

COMBIESCO, D., DUMITRESCO, N. & COTĂESCO-MANCIULESCO, E., Mme. Recherches sur le typhus exanthématique. L'influence de la splénectomie sur la réceptivité des animaux de laboratoire à l'infection expérimentale typhique. [**The Influence of Splenectomy on the Susceptibility of Animals to Experimental Typhus Infection.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 91–103, 13 charts.

The spleens of five guineapigs were removed at periods ranging from 30 to 138 days after experimental attacks of typhus fever. Four to ten days after the operation the animals were challenged by a second inoculation with typhus infection ; four reacted in the same way as normal control guineapigs and one was immune.

In similar experiments on five rabbits it was found that two had lost their immunity after splenectomy and three did not react to the challenge of reinoculation. *John W. D. Megaw*

COMBIESCO, D., DUMITRESCO, N., STURDZA, Nina & BOTEZ, V., Mme., with the collaboration of C. POPESCO, G. PANAITESCO & C. ZILISTEANO. Recherches sur le typhus exanthématique. Étude sur l'immunité acquise. Efficacité comparative de trois vaccins tués. Propriétés sérologiques des sujets vaccinés. [**A Serological Study of the Immunity caused by three Killed Typhus Vaccines.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 68–90, 4 graphs & 1 fig. [23 refs.]

Tests were carried out at fixed intervals on the sera of three groups of 24–25 men vaccinated with a yolk-sac, a mouse-lung, and a dog-lung typhus vaccine respectively. The number of *Rickettsia prowazeki* in each type of vaccine was approximately the same.

No significant difference in the antigenic activity of the three vaccines was observed.

In the combined results of Weil-Felix tests the percentages of positive reactions at titres of 1–100 to 1–250 were :—before vaccination, 2·7 ; thirty days after vaccination, 67·2 ; sixty days after vaccination, 40·0 ; and ninety days after vaccination, 2·3. In 20 per cent. of the cases the reaction remained negative at 1–50 throughout the period.

With the Kudicke and Steuer dry-blood rapid agglutination test [see this *Bulletin*, 1943, v. 40, 898] negative reactions were always obtained, though this test was always positive in cases of typhus in which the Weil-Felix titre was higher than 1–250.

The intradermal rabbit test of Giroud was carried out on sera of 46 of the men ; in six cases there was some degree of " neutralizing power " before vaccination ; in 33 a considerable degree of neutralizing power was acquired after vaccination, and in two the reaction was moderately positive before and after vaccination. No significant difference was observed in the responses observed after vaccination with the three different vaccines. There was no correlation between the results of the Giroud and the Weil-Felix tests ; often one was positive and the other negative. When both were positive the times of appearance of the reactions were different and the Weil-Felix reaction remained positive longer than the Giroud which always became negative before the 60th day. The authors regard these results as being additional evidence that the protective antibodies are independent of the anti-*proteus* agglutinins.

[The rapid disappearance of the antibodies concerned in the Giroud reaction suggests that they are not the substances responsible for giving durable protection against typhus fever.] *John W. D. Megaw*

DENT, J. E., MORLAN, H. B. & HILL, E. L. **Effects of DDT Dusting on Domestic Rats under Colony and Field Conditions.** *Pub. Health Rep.* Wash. 1949, May 27, v. 64, No. 21, 666–71, 1 chart.

A colony of rats was exposed to conditions similar to those occurring when DDT dust is used for the control of rat fleas. By the end of three weeks 24 of the rats had died. The liver and fat of the dead rats contained enough DDT to account for death. Within 11 weeks, 36·3 per cent. of the rats died, apparently of DDT poisoning, but it is stated that general field observations indicate that this rate is in excess of what can be expected under conditions in which the rats have greater opportunities of avoiding contact with the dust.

No mention is made of the occurrence of births in the colony which consisted originally of 43 male, 50 female, and 20 baby rats. The only comment on the effect of the procedure on the rat population is the statement that DDT dusting " affected this directly". *John W. D. Megaw*

DERRICK, E. H. & BROWN, H. E. **Isolation of the Karp Strain of *Rickettsia tsutsugamushi*.** *Lancet.* 1949, July 23, 150–51. [13 refs.]

The Karp strain of *Rickettsia tsutsugamushi* (*R. orientalis*) well deserves a biographical note. It was isolated by the authors at Brisbane in January, 1943, by inoculating a guineapig with the blood of an American soldier called Karp who had been infected in New Guinea before being evacuated to Australia. The guineapig had a sharp febrile attack which started 10 days after inoculation and the strain was readily passed through other guineapigs, none of which died during the first nine passages, but thereafter about 50 per cent. of the inoculated guineapigs succumbed.

In its pathogenicity to the originally inoculated guineapig the strain differed from Malayan and other strains. It has been very extensively used in the experimental study of scrub typhus; for example in 1945 by such workers as TOPPING, FULTON and JOYNER, and BENGTSON, and since that time by many other workers.

It has been responsible for a considerable number of laboratory infections already noted in this *Bulletin*, including the tragic fatal illness of Miss Dora LUSH at the Melbourne Laboratory in 1943. *John W. D. Megaw*

SMITH, C. N., COLE, M. M. & GOUCK, H. K. **Biology and Control of the American Dog Tick.** *U.S. Dept. Agric. Tech. Bull. No. 905.* Wash. 1946, 74 pp., 37 figs. [21 refs.]

DE MAGALHÃES, O. Profilaxia do tifo exantemático neotrópico no Brasil. [**Prevention of Neotropical Exanthematic Typhus in Brazil.**] *Rev. Hig. e Saúde Pública.* 1948, Apr.–Dec., v. 6, Nos. 2, 3 & 4, 169–76.

The author describes the measures needed for the control of tick-borne typhus in Brazil; he refers to the bed-bug as being a transmitting vector in addition to the ticks *Amblyomma cayennense* and *A. brasiliense*. The methods of control recommended are:—destruction of the vector arthropods and of animals known to be reservoirs of infection, especially dogs and goats; propaganda by cinema, posters, leaflets, and lectures; and vaccination by yolk-sac vaccines.

It is suggested that in addition to the very severe cases to which special attention has been paid there are also mild and even inapparent attacks during "silent" periods and in areas in which the disease is not detected. The mild attacks may be caused by transmission by bed-bugs or by strains of rickettsiae of low virulence transmitted by ticks; it is believed that in certain areas the population has been immunized by these mild attacks, so it is doubtful whether yearly vaccination would be of sufficient value to justify the maintenance of an expensive organization. *John W. D. Megaw*

COMBIESCO, D., VASILIU, V. & DUMITRESCO, N. Identification d'une nouvelle Rickettsiose chez l'homme en Roumanie. [**Identification of a New Human Rickettsial Disease [Q fever] of Rumania.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 230–32.

See this *Bulletin*, 1949, v. 46, 627.

COMBIESCO, D. & DUMITRESCO, N. Survivance "in vitro" des rickettsias isolées chez les malades de la nouvelle rickettsiose identifiée chez l'homme en Roumanie. [**Survival *in vitro* of *Rickettsia burneti*, isolated in Rumania.**] *Arch. Roumaine Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 261–3.

See this *Bulletin*, 1949, v. 46, 627.

COMBIESCO, D., DUMITRESCO, N., STURDZA, Nina, BOTEZ, V., Mme., CIUREA, V. & ZARNEA, G. Recherches expérimentales sur la nouvelle rickettsiose isolée en Roumanie. [**Investigations into the New Rickettsial Disease [Q Fever] of Rumania.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 242–4.

The author describes briefly the reactions produced in guineapigs inoculated with the strain of *Rickettsia burneti* isolated from Q fever patients in Rumania. The rickettsia survived in guineapigs up to 64 days. None of the 50 guineapigs employed in the course of 14 transfers died. The chief lesions found in guineapigs sacrificed on the 4th day of the fever were great enlargement of the spleen and extensive congestion with mononuclear-cell infiltration of the interalveolar tissues of the lungs. *John W. D. Megaw*

COMBIESCO, D., COMBIESCO, Cornelia, DUMITRESCO, N., POPESCO, C. & ZARNEA, G. Diagnostic rétrospectif, par la réaction de fixation du complément, d'un nouveau foyer de la maladie provoquée par la nouvelle rickettsiose identifiée en Roumanie. [**Retrospective Diagnosis of a New Focus of Q fever in Rumania.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 264–5.

See this *Bulletin*, 1949, v. 46, 627.

COMBIESCO, D., DUMITRESCO, N., BOTEZ, V., Mme., STURDZA, Nina & ZARNEA, G. Infections de laboratoire avec la nouvelle rickettsiose isolée en Roumanie. [**Laboratory Infection with the New Rickettsial Disease [Q Fever] of Rumania.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1948, v. 15, Nos. 1/2, 244–7.

Three of the workers engaged in the manipulation of material infected with *Rickettsia burneti* suffered from attacks of Q fever. The diagnosis was confirmed by complement-fixation tests in which an Australian and a local antigen were used.

Infection was believed to have been acquired by the inhalation of infected droplets. *John W. D. Megaw*

WOLFE, D. M. & KORNFELD, Lottie. **The Application of a Quantitative Complement-Fixation Method to a Study of Q Fever Strain Differentiation.** *J. Immunology.* 1949, Apr., v. 61, No. 4, 297–306. [18 refs.]

Several workers have observed disconcerting differences in the complement-fixing antigens of various strains of Q fever rickettsiae [see this *Bulletin*, 1949, v. 46, 726.]

The authors found that when fixation tests were carried out in the usual way, by the "serum dilution" or "antigen dilution" method, the reactions with the American (Dyer) strain of antigen were at much lower titres than those obtained with the Italian (Henzerling) or the Australian strain.

A series of tests was made with the quantitative complement-fixation technique developed by the Division of Laboratories and Research of the New York State Department of Health. The technique is much too complicated for general use; the underlying principle is that all reactions are evaluated in terms of the amount of complement needed for 50 per cent. haemolysis [see this *Bulletin*, 1946, v. 43, 210; and 1947, v. 44, 654].

Twenty sera of persons infected in America, Italy, Germany, and Switzerland were tested and the titres observed were not significantly different in any serum irrespective of whether the antigen used was of American or Italian origin.

John W. D. Megaw

CAUGHEY, J. E. **A Preliminary Report of a Search for Q Fever in New Zealand.** *New Zealand Med. J.* 1949, Apr., v. 48, No. 264, 174–9. [16 refs.]

No evidence of Q fever infection was found in any of four patients treated at the Auckland hospital for primary atypical pneumonia. Blood from three of the patients, taken at the height of the fever, was inoculated intraperitoneally into guineapigs with negative results, and the sera of the patients, examined 25 to 47 days after the attack gave negative reactions to agglutination tests against *Rickettsia burneti.*

Agglutination tests, carried out on 11 abattoir workers and 12 dairy farmers in places where *Haemaphysalis bispinosa* was common, also gave negative results. *John W. D. Megaw*

BOWER, A. G. **Q Fever.** *Arizona Med.* 1949, May, v. 6, No. 5, 30–33. [31 refs.]

The clinical features of Q fever in California are briefly described. Pulmonary lesions occur in 80 per cent. of the cases and in these differentiation from primary atypical pneumonia is impossible on purely clinical grounds though early and frequent chills are in favour of Q fever.

The severity ranges from mild ambulatory attacks, in which the patient feels ill for one or two days, to a prolonged severe illness needing hospital treatment for a month or more. The average duration is 7 to 11 days.

Streptomycin was effective in daily quantities of 2 to 3 gm. given intramuscularly in six divided doses during the febrile period, and in half these doses for the next two to four days.

Aureomycin is said to be specific: it is given by the mouth in total daily doses of 50 mgm. per kgm. body weight, but it is very costly at present.

Infection is believed to be acquired chiefly by inhaling infected dust from material contaminated by the urine or dung of cattle, but drinking infected milk is also a mode of transmission. *John W. D. Megaw*

YELLOW FEVER

MAHAFFY, A. F. **The Epidemiology of Yellow Fever in Central Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, May, v. 42, No. 6, 511–24, 2 maps. [27 refs.] Discussion 525–30 [FINDLAY, G. M.; MATTINGLY, P. F.; MACGRAITH, B.; GARNHAM, P. C. C.; HACKETT, C. J.; RAE, W.; MORGAN, M. T.; MAHAFFY, A. F. (in reply)].

In 1936 a team of workers under Mahaffy commenced a study of the epidemiology of yellow fever in Central Africa. In the course of the following 12 years this group has made many contributions to our knowledge of the subject and in addition has found at least eight new viruses.

Practically all the studies of Mahaffy and his colleagues were made in Bwamba County, Uganda which is a small, heavily forested area. The main forest (Semliki) is closed to human habitation but about 35,000 people live in a cultivated zone between it and a large mountain range. Mosquitoes, monkeys and man were all examined for virus and most of the results have been described in detail already in a number of papers which have been fully abstracted in this *Bulletin.*

The main point made by Mahaffy was that in this area yellow fever appeared to be primarily a disease of primates with *Aëdes africanus* as the chief vector in the forest. All attempts to isolate virus from other mosquitoes in the course

of their investigation were unsuccessful. Arboreal monkeys, however, raid the human plantations for food and may be bitten by *A. simpsoni* which then transmits the disease to man. *A. simpsoni* may on occasion also enter the forest for a blood meal and bite an infected monkey. Although *A. aegypti* occurs in this region it apparently plays no part in the cycle. The naturally infected monkeys seldom die and they travel only very short distances.

In discussion of Dr. Mahaffy's paper it was mentioned that there was a lot of evidence which suggested that the forest type of the disease exists in West Africa and that monkeys play as important a part as vertebrate hosts but the forest vector has not yet been found in that region. Mahaffy said he regarded it as extremely unlikely that the control of either the animal host or the forest vector could be undertaken with any reasonable hope of success. Persons exposed to the sylvan type of the disease can, however, be protected against it by vaccination. *F. O. MacCallum*

HOVANITZ, W. **Comparisons of Mating Behavior, Growth Rate, and Factors influencing Egg-hatching in South American *Haemagogus* Mosquitoes.** *Physiol. Zoöl.* Chicago. 1946, v. 19, No. 1, 35–53, 5 figs. [18 refs.]

RABIES

JERVIS, G. A. & KOPROWSKI, H. **Encephalomyelitis of possible Allergic Etiology in Mice injected with Rabies Vaccine.** *Canadian J. Comp. Med.* 1949, May, v. 13, No. 5, 116–21, 3 figs. [21 refs.]

Occasionally paralysis of limbs has been observed in mice after vaccination with the Semple type of rabies vaccine. Thus, in the experiment described in the present article, 55 Swiss mice were employed in testing, by Habel's method, the potency of a phenolized, wholly inactivated, rabies vaccine, prepared from horse-brain tissue infected with rabbit-brain fixed virus; 2 animals developed a paralysis which, beginning in the posterior limbs, gradually extended to the anterior limbs.

In the paralysed mice, sacrificed one month after the appearance of first symptoms, the pathological lesions occurred almost exclusively in the white matter of the central nervous system as multiple, small areas of demyelination and perivascular infiltrations distributed throughout the spinal cord, cerebellum and midbrain; they were unlike those caused by mouse encephalomyelitis virus (typically inflammatory reactions localized in the grey matter, absence of demyelinating areas), but closely resembled those obtained in guineapigs after injection of rabbit brain with adjuvants. Inasmuch as the mice in the present study received inoculations of brain tissue without adjuvants, however, the conditions of the experiment approximated to those in human subjects receiving repeated injections of rabies vaccine, even if the total dosage per kilogramme of body weight in mice was 25 times that in man.

In their summary the authors suggest that the lesions found in the paralysed mice may have been due to an allergic reaction to an antigen in the horse-brain tissue present in the rabies vaccine. The similarity of this pathological picture to that previously described in the guineapig under similar experimental conditions is stressed and its bearing on post-vaccinal encephalitis in human subjects receiving anti-rabies treatment is indicated. *G. Stuart*

PLAGUE

SEAL, S. C. **Pneumonic Plague Cases in Calcutta and Gaya.** *Indian Med. Gaz.* 1949, Apr., v. 84, No. 4, 162–70, 1 fig. & 2 charts. [15 refs.]

Between March 25th and April 7th, 1948, twelve members of a family community of 31 persons were attacked with pneumonic plague, and two other persons who had come into close contact with the patients were also attacked. Only one of the patients survived; he was treated with streptomycin in a Calcutta hospital.

Infection was introduced by a member of the family who had arrived from a plague-infected locality on the day of onset of his illness. Four days later two attacks occurred and during the following three days there were seven more cases. After an interval of three days the remaining four patients were attacked within a period of three days. No further cases occurred although large numbers of persons came into close contact with several of the patients attacked during the latter stage of the outbreak; some of these patients had fled from the infected household during the incubation period and others were admitted to hospitals where the nature of their illness was not at first recognized.

The incubation period was usually about two days; death occurred in most of the cases within two or three days; in two cases the patients died after an illness of five days. Signs of lung involvement were not striking, there was little sputum and this was blood-stained in only one case.

A brief reference is made to another outbreak at Gaya, Bihar, in which a homoeopathic doctor became infected while attending a group of six pilgrims who had become infected in a distant locality where plague was occurring. Ten members of the doctor's family of 18 persons were attacked and died in rapid succession.

These outbreaks were typical of plague pneumonia as it occurs in India. The author quotes the records of nine outbreaks which occurred in Eastern Bengal between 1898 and 1911; the number of cases ranged from 4 to 51, and all but one was in a locality where plague had not occurred. The Indian Plague Commission of 1908 is quoted as stating that only about 3·0 per cent. of the cases of plague in India were of the pneumonic type.

[The rapid and spontaneous termination of these dramatic outbreaks suggests that when infection is transmitted from man to man by droplet infection the organisms soon lose their virulence. Another interesting feature of plague pneumonia is that although many outbreaks have occurred in plague-free areas there is no record of the establishment of infection among the rats of the affected localities. In India at any rate, the outbreaks, though tragic, appear to be self-limited and to be of little epidemiological importance.]

John W. D. Megaw

POLLITZER, R. **Recent Trends in the Treatment and Control of Plague.** *Acta Tropica.* Basle. 1949, v. 6, No. 1, 30–40. [23 refs.]

This is a valuable critical summary of recent advances in connexion with the treatment and control of plague. In treatment the sulphonamides have proved their value; sulphadiazine and sulphamerazine are specially recommended because they can be given intravenously in severe cases.

Streptomycin, given alone or as a supplement to sulphonamide treatment, has given still better results. Serum can be expected to add to the efficacy of the treatment, especially if the new purified rabbit serum can be made available. The above lines of treatment may save the lives of some pneumonic-plague patients.

Great importance is attached to the use of sulphonamides as prophylactics for persons who have come in contact with patients suffering from pneumonic plague, but the method is not recommended for general use in bubonic plague. Killed vaccines are of undoubted value, especially when the two-dose method is adopted and booster doses are given later when risk of infection persists. Living attenuated vaccines may become suitable for general use if they can be made available in stable, lyophilized, form ; so also may purified crystalline antigens.

Flea control by DDT, and inoculation, are the methods of control most generally applicable in the presence of infection. The elimination of rats is the ideal method of long-term control.

Treatment of patients in their own homes or in village emergency hospitals should be far more widely carried out than is the case at present.

John W. D. Megaw

RUEGSEGGER, J. M. & GILCHRIST, H. **The Present Outlook in Plague.** *Indian Med. Gaz.* 1949, Apr., v. 84, No. 4, 159–61. [22 refs.]

This article is on the same lines as the above, but the authors have not had the advantage of personal experience in the field.

A prediction is made that when more potent and less expensive antibiotics become available plague vaccines will lose their popularity.

[In reaching this opinion the authors have probably been influenced by certain recent reports which are regarded by most experts as having conveyed an unduly pessimistic impression of the efficacy of vaccines.]

John W. D. Megaw

CHOLERA

i. BROUNST, G. & MAROUN, T. Recherche d'anticorps chez des sujets vaccinés contre le choléra. [**Agglutinin Levels after Inoculation against Cholera.**] *Ann. Inst. Pasteur.* 1949, June, v. 76, No. 6, 554–7.

ii. GALLUT, J. & BROUNST, G. Sur la mise en évidence des agglutinines cholériques. [**Demonstration of Agglutinins in Cholera.**] *Ibid.*, 557–9.

i. The agglutinin levels produced by inoculation with anti-cholera vaccine were determined in 486 military subjects. A first series of sera was taken from 371 subjects 20 to 60 days after inoculation with a single dose of a vaccine containing equal parts of Inaba- and Ogawa-type strains at a total dosage of 2,000 million vibrios. The tests were made against suspensions of *V. cholerae* in 0·2 per cent. formol-saline. Of the 371 sera, 365 were negative at a dilution of 1 in 25 ; 6 (1·6 per cent.) were positive at dilutions of 1 in 25 to 1 in 100 only.

A second series of tests was made on sera of 95 subjects who, in addition to the initial dose of 2,000 million vibrios, received two additional doses of the vaccine bringing the total to 14,000 million. At the same period after inoculation, 84 sera gave negative results and 11 (11·5 per cent.) were positive at dilutions of 1 in 25 to 1 in 100.

In view of the mediocre results obtained in the above tests live suspensions of *V. cholerae* were used for tests of a third series of 20 sera of persons given the same course of inoculation as the second series. Of these 13 were negative and 7 (35 per cent.) were positive at 1 in 25 to 1 in 200.

Local reaction to intradermal injection of 0·1 cc. of anti-cholera vaccine was tested in 10 immunized subjects; 5 showed redness and swelling of some degree, with or without a zone of necrosis or palpable nodule at the site of the injection.

The results are considered to show that the production of agglutinins in persons inoculated with anti-cholera vaccine is exceptional and less frequent than is generally supposed: the use of formalinized suspensions for the test will reduce the number of positives obtained. The test for intradermal reaction may be useful for demonstrating evidence of immunity.

ii. Following on the work reported above a comparison was made in more detail of the results of agglutination tests with living and formalinized suspensions of *V. cholerae*. The living suspensions were used fresh and the formalinized after being kept for 24 hours and for 7 days. The sera of 18 persons inoculated with the same total of 14,000 million vibrios were examined. Against live Inaba suspensions 8 were negative, 6 positive at 1 in 20, 1 positive at 1 in 50, 2 positive at 1 in 100 and 1 positive at 1 in 500. Against live Ogawa suspensions 4 were negative, 6 positive at 1 in 50, 7 positive at 1 in 20 and 1 positive at 1 in 500. With formalinized suspensions kept 24 hours before use only 3 gave positive results with the Inaba strain and 2 with the Ogawa strain, the titres being 1 in 20 to 1 in 50. When the suspensions were kept 7 days before use two only gave positive results with Inaba and one with Ogawa suspension, at the same low levels.

Additional tests were carried out with anti-O cholera diagnostic sera prepared in rabbits and showing titres of 1 in 10,000 with the homologous type strain, when living suspensions were employed. Titres with formalinized suspensions were only about one-quarter of those obtained with living suspensions.

The authors conclude that it is essential to use live suspensions for agglutination tests on the sera of inoculated persons, for the purpose of demonstrating the presence of antibodies, on account of the very low titre usually reached.

[This is the usual method employed by experienced cholera workers.]

J. Taylor

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

ADAMS, A. R. D. & SEATON, D. R. **Amoebiasis in England as a Household Disease.** *Brit. Med. J.* 1949, July 16, 136.

Isolated cases of autochthonous amoebic infection have been recorded in Britain, but for the most part without regard to the source of infection or of infectivity to contacts. The authors now refer to three families in Liverpool in each of which more than one member was suffering from amoebiasis. The original cases were seen in July 1947, July 1948 and February 1949 respectively.

The first case was that of a ship's officer who had had proved amoebic dysentery for a few weeks: his wife, who had not been overseas, had recently developed diarrhoea and examination of her stools showed that she had active amoebic dysentery.

The second case was in a boy of 16 who had undetermined dysentery intermittently for two years. Numerous vegetative *E. histolytica* were found in the stools. He had been all his life in a Liverpool slum, as had all the other 8 members of his family. The boy's mother had had diarrhoea for two months and stool examination showed that she had acute amoebic dysentery. The

stepfather and four of the six other children were passing *E. histolytica* cysts, but were in good health. The family was also largely infected with *E. coli*, *Giardia* and threadworms.

The last case was that of a boy of 7 with an intractable colitis for three years: very large numbers of vegetative *E. histolytica* were found in the stools. He had never lived out of Liverpool. Stools from five other members of the family were negative, except those of his stepfather who was passing *E. histolytica* cysts: he had no history of dysentery but had been in India until he was 13 (he is now 45) and had lived in England ever since.

The authors point out that these experiences are a reminder that amoebiasis may easily spread in households where personal cleanliness is not high. They stress the necessity of excluding amoebic dysentery by microscopic examination before ulcerative colitis is diagnosed. The possibility of the former condition being present is not perhaps considered sufficiently in Britain: yet two of the patients referred to above had been ill for years and were in poor health for want of proper diagnosis which earlier microscopic examination would have readily provided. *H. J. O'D. Burke-Gaffney*

GAEHLINGER, H. La dysenterie amibienne, maladie d'association parasitaire et microbienne. [**Amoebic Dysentery as a Combined Parasitic and Bacterial Disease.**] *Bruxelles-Méd.* 1949, June 5, v. 29, No. 23, 1255–60.

Some authors attribute the pathogenicity of *Entamoeba histolytica* solely to the parasite, others consider it dependent on an association with certain bacterial concomitants. The author, on the evidence, considers it certain that amoebic dysenteric manifestations are aggravated by concurrent bacterial infections. Reviewing the history of the treatment of amoebic dysentery he refers to the failure of emetime to sterilize the infection, and he considers that drugs like the iodoquinolines, rivanol, benzo-metacresol and the pentavalent arsenicals, all of which exert some amoebicidal action, have an antiseptic action. Emetine itself is not only an amoebicide but it promotes the agglutination and phagocytosis of pyogenic micro-organisms. These facts support the view that concomitant bacterial infections play their rôle in determining the pathogenicity of an amoebic infestation, and the remarkable success of the emetine-penicillin-sulphaguanidine treatment of severe amoebiasis confirms this. There is no evidence, the author suggests, that non-pathogenic strains of *E. histolytica* exist, or of the existence of *E. dispar* as a separate species. The apparently non-pathogenic strains of amoebae rapidly become pathogenic in a suitable bacterial environment. The conditions for this are prevalent in the human bowel in hot moist countries, and less so in cold temperate climates. *A. R. D. Adams*

PIPKIN, A. C. **Experimental Studies on the Role of Filth Flies in the Transmission of** *Endamoeba histolytica*. *Amer. J. Hyg.* 1949, May, v. 49, No. 3, 255–75. [26 refs.]

The author re-examines the rôle of flies as disseminators of *Entamoeba histolytica*, the causative organism of amoebic dysentery. Instructive results are obtained by a comparison of the ability of *Musca domestica*, *Lucilia pallescens*, *Cochliomyia macellaria*, *Phormia regina* and *Sarcophaga misera* var. *sarracenoides* to carry cysts and vegetative forms on the external parts of the body, in the crop, midgut and hindgut, or to deposit them in the vomit or in the faecal drops. At various intervals after clean, laboratory-bred flies of each species had fed on a highly infected faecal pabulum, direct observations were made

on washings or on dissections of the flies and a parallel series of cultures were set up from the same material. Vomit drops and faecal drops were taken up in micropipettes and examined by similar means.

Culturable trophozoites did not persist on the external surfaces of flies for more than 1·5 minutes after contact with infected material. Trophozoites were, however, culturable after 40 minutes in the crop and 30 minutes in the midgut but none were cultured from the rectum although they were seen by direct observation in this region 10 minutes after the meal.

Cysts survived longer than the trophozoites. On the external parts of the body they persisted in culturable form for up to 4 minutes and for as long as 210 minutes in the crop, 240 minutes in the midgut and 210 minutes in the rectum.

In the vomit drop, trophozoites were obtained in culturable form for up to 17 minutes and culturable cysts for 64 minutes after the infecting meal. Faecal drops contained culturable cysts for as long as 254 minutes.

Detailed figures are provided in elaborate tables and a comprehensive statistical analysis of the data shows that there is, in fact, a tendency for both trophozoites and cysts to survive longer in the crop than in the midgut or rectum of all the species of fly. This amoebicidal effect, apparent only in the midgut and rectal region of the flies was not more marked in one species than in another. Cysts survived the passage through the gut better than did the trophozoites.

The number of flies vomiting infective drops was substantially the same for each species. On the other hand, the total number of infective vomit drops varied significantly with the species; the larger species continued to vomit culturable cysts for longer periods than the smaller species. This is attributed to the larger capacity of the crop of the larger flies. There was, however, less evidence to suggest that the length of the gut affected the length of time during which infective faeces could be deposited.

It is concluded that the passage by flies of viable cysts in their vomit drops and in their faeces are the two most likely methods by which they could play a part in the spread of amoebic dysentery. External carriage of any form of the amoeba and the deposition of trophozoites in the vomit or in the faeces are considered to be mechanisms of minor importance. *D. S. Bertram*

Ortuzar E., R. & Montero O., E. Amoebiasis crónica y apendicitis. [**Chronic Amoebiasis and Appendicitis.**] *Rev. Med. Chile.* 1949, Feb., v. 77, No. 2, 105–12, 5 figs. [27 refs.]

The authors point out how often the appendix may be invaded by *E. histolytica* and quote the figures given by Faust of 249 cases in which the appendix came a close second to the caecum as the site most involved, 32·1 and 33·3 per cent. respectively. They relate details of a few chosen examples where the diagnosis was by no means easy and the symptoms were those of appendicitis, acute or chronic, and in one the operation of appendicectomy was undertaken. Diagnosis may need the help of a detailed study of the history, rectoscopy, faecal examination, complement fixation and radiological examination after administration of a barium enema. *H. Harold Scott*

Singh, B. **Two Cases of Amoebic Liver Abscess with Complications.** *Indian Med. Gaz.* 1949, Apr., v. 84, No. 4, 147–9.

"The post-mortem findings of two cases of amoebic liver abscess with complications are described. Case 1 had no history of amoebic dysentery. The

abscess in the liver was situated on the posterior aspect of the left lobe. Pin-point amoebic ulcers were found in the upper part of the descending colon only. The liver showed a typical amoebic abscess but amoebae could not be demonstrated in histological sections. The abscess in the lung as well as the pin-point ulcers in the descending colon showed amoebae in large numbers. Case 2 was admitted to hospital with amoebic dysentery. At autopsy no dysenteric ulceration of the gut was to be seen. He had an encysted liver abscess as well as an encysted abscess of the spleen, abscess of the lung and a cerebral abscess showing secondary infection. No amoebae could be demonstrated in any of the abscesses."

DAVIS, F. W., Jr. **Amebiasis : Experience in the Johns Hopkins Hospital, 1936–1946.** *Amer. J. Med. Sci.* 1949, May, v. 217, No. 5, 505–17. [50 refs.]

Between 1936 and 1946, 296 in-patients at the Johns Hopkins Hospital were said to suffer from amoebiasis ; of these only 205 were diagnosed parasitologically, and these accounted for 0·51 per cent. of all admissions to the medical wards during this period. The author has analysed the data relevant to these cases in the light of the considerable literature on the subject. The protean nature of the symptomatology and physical findings in amoebiasis is re-emphasized ; diarrhoea and abdominal tenderness proved the most constant features. The iodoquinoline compounds are advocated in the treatment of uncomplicated amoebiasis, emetine being reserved for severe cases and those with extra-intestinal involvement. In resistant cases combinations of drugs may be used, but the preparations employed are of less consequence than their administration for an adequate period. Twenty-five per cent. of the patients continued to suffer from symptoms after treatment, although the stools no longer contained parasites ; a true post-amoebic ulcerative colitis developed in only 5·9 per cent. of the cases.

[This paper covers a wide field and gives a restrained and well-balanced account of the subject ; it should be consulted in the original by those interested.] *A. R. D. Adams*

MALHOTRA, S. L. **Causes of Failure in Treatment of Amoebic Dysentery.** *Indian Med. Gaz.* 1949, Mar., v. 84, No. 3, 96–8.

In spite of improved methods resulting from war experience, the apparent cure-rate after treatment of amoebiasis in India, where the infection is very prevalent, is still unsatisfactory. Possible reasons for this are examined and the author suggests that in re-infection from the faecally contaminated fingers of the patient or from those of carriers in the household, and not in persistence of the infection, lies the real explanation. *A. R. D. Adams*

BROUGHTON, N., OGILVIE, A. C. F. & WYLIE, W. D. **Diagnosis and Treatment in Latent Amoebiasis with special reference to Cases presenting with Pyrexia alone.** *J. Trop. Med. & Hyg.* 1949, June, v. 52, No. 6, 112–20.

The authors observed 676 cases of amoebiasis in Aden between February and November 1947 ; most of these were free from symptoms. The diagnosis was based on recovery of the parasite by stool examination before or "after a provocative dose of emetine with or without purgation" ; sigmoidoscopy was a routine unless refused by the patient, but infection was detected solely by this means in only three cases. The clinical and pathological findings are discussed in some detail as the authors were impressed by their mildness or

absence in so many cases, an aspect of amoebiasis to which they believe inadequate attention is directed in the textbooks. They consider stool re-examination is desirable for all persons returning from the highly endemic areas to the United Kingdom ; as carriers (" symptomless cases ") all have lesions in the gut they need treatment both for the sake of themselves and to prevent dissemination of the infection to others. The treatment given by the authors followed conventional lines. *A. R. D. Adams*

BATTERSBY, A. R. & OPENSHAW, H. T. **Studies on the Structure of Emetine. Part I. The Hofmann Degradation.** *J. Chem. Soc.* 1949, Suppl. Issue No. 1, 59–67.

BATTERSBY, A. R. & OPENSHAW, H. T. **Studies on the Structure of Emetine. Part II. Oxidation with Mercuric Acetate, and the Properties of Rubremetinium Salts.** *J. Chem. Soc.* 1949, Suppl. Issue No. 1, 67–71.

NORCROSS, G. & OPENSHAW, H. T. **Studies on the Structure of Emetine. Part III. Stability of some α-Arylalkyl-trimethylammonium Iodides.** *J. Chem. Soc.* 1949, May, 1174–9.

DO PRADO, F. C. Tratamento da amebíase. [**Treatment of Amoebiasis.**] *Hospital.* Rio de Janeiro. 1947, Mar., v. 31, No. 3, 431–40. English summary.

After preliminary remarks on the various drugs employed in the treatment of infection by *E. histolytica*—emetine hydrochloride, enterovioform, yatren, carbarsone, enterostovarsol, etc., and adjuvant drugs such as sulphaguanidine, bacteriophages, vaccines and care in diet—the author refers to 140 selected cases of his own which he treated with iodine preparations (iodoquinoleine) and pentavalent arsenicals in alternate weeks for a total of four months. He followed them up for a year or more and groups the results as follows : 98 were cured ; amoebae were no longer found and the clinical symptoms cleared up ; 24 still had attacks of diarrhoea or intestinal disturbance, although the amoebae could no longer be found. The remaining 18 presented signs of a more or less chronic colitis with relapses or exacerbations, such as general depression, easy fatigue, transitory pain in the liver region, intolerance of certain foods, although faecal examination failed to reveal any entamoebae.

H. Harold Scott

KNIGHT, Alva A. & MILLER, Jeanne. **Comparative Studies on the Iodine Absorption of Anayodin, Chiniofon, Diodoquin, and Vioform in Man.** *Ann. Intern. Med.* 1949, June, v. 30, No. 6, 1180–87, 1 fig. [11 refs.]

All these substances are iodo-hydroxyquinolines. Anayodin is the same as chiniofon (also known as quinoxyl and yatren). Diodoquin and vioform differ from chiniofon by absence of the sulphonic acid group ; diodoquin has two iodine substituents, while vioform has one iodine and one chlorine.

Since direct methods of assay of these drugs are not available, their absorption after oral treatment was studied indirectly by determining blood iodine levels. The studies, involving a total of 280 estimations, were made on 36 patients under ambulatory treatment for amoebiasis, the treatment being in the usual therapeutic dosages, administered daily. In all cases a peak of blood concentration was reached before the seventh day of treatment, and there was no evidence of cumulative absorption or toxicity. The recommended

therapeutic dosage of diodoquin gives the highest iodine blood levels, anayodin and chiniofon the lowest, while vioform gives intermediate values. However if absorbability be measured by relating the blood levels to iodine intake, then vioform ranks highest, diodoquin second, and anayodin and chiniofon third.

Evidently none of these compounds is wholly non-absorbable, as has previously been stated in connexion with diodoquin, and the fact that "reasonable" iodine blood levels are attained raises a question as to the effectiveness of these drugs on amoebae deep in the walls of the intestine or in other parts of the body. "If therapeutic value is dependent on iodine absorption, Diodoquin, Vioform and Anayodin or Chiniofon would rank in the order given in therapeutic effectiveness."

E. M. Lourie

GAN, K. H. Bijdrage tot de kennis van de amoeben bij ratten. [**Contribution to the Knowledge of the Amoebae in Rats.**] *Med. Maandblad.* Batavia. 1949, Mar. 1, v. 2, No. 3, 70–76. [12 refs.] English summary.

The author describes two kinds of amoebae found in laboratory rats and in wild *Rattus rattus diardi*, in Batavia. One of these amoebae is said to resemble *Entamoeba histolytica*, while the other is *E. muris*. Both occur in the caecum of the rats.

In *E. muris* the ectoplasm is not clearly demarcated from the endoplasm, and the movements are sluggish. Its general appearance is like that of *E. coli*, but, according to the author, it can be distinguished from the latter (1) by the smaller size of its cysts, and (2) by the structure of its nucleus, in which the peripheral chromatin granules are arranged in the form of a complete ring instead of an interrupted ring. The author saw only binucleate cysts with a large glycogen vacuole in *E. muris*.

The *histolytica*-like entamoeba is active, its pseudopodia are protruded rapidly, and the ectoplasm is clearly separated from the endoplasm. The nucleus is conspicuous in unstained amoebae; and in stained preparations the peripheral chromatin granules appear in the form of an interrupted ring, which is said to be a characteristic of *E. histolytica*, while the karyosome (the author's "chromatin mass") may be central or eccentric. Only binucleate cysts were seen, in which there was a large vacuole displacing the nuclei to the periphery.

The food-vacuoles in both amoebae contained bacteria. On addition of rat blood to samples of faeces containing the amoebae, the *histolytica*-like form readily ingested erythrocytes, whereas *E. muris* was less inclined to do so. Attempts to infect kittens with both kinds of the rat amoebae were unsuccessful. The paper is illustrated by photomicrographs and schematic figures illustrating the two types of entamoebae seen in rats.

[The characters adduced for the *histolytica*-like amoeba, especially its nuclear structure and cysts, are not peculiar to *E. histolytica*, the presence of which in the author's material is therefore somewhat doubtful. It is more probable that both the amoebae described in this paper represent *E. muris*.]

C. A. Hoare

COUTELEN, F. COCHET, G. & BIGUET, J. Fréquence du parasitisme à *Giardia intestinalis* chez les enfants, agés de deux à six ans, de la région du Nord. [**Frequency of *Giardia intestinalis* Infection in Children of Two to Six Years in the North of France.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 3/4, 103–6.

Systematic stool examinations, 5,403 in all, were made in specimens from 1,915 apparently healthy children in kindergarten schools in the Nord region.

Among these 629 (32·84 per cent.) harboured *Giardia intestinalis*: this incidence is one of the highest recorded among children in temperate regions.

H. J. O'D. Burke-Gaffney

SIRKER, M. U. **Two Atypical Cases of Giardia Infection.** *Indian Med. Gaz.* 1949, Mar., v. 84, No. 3, 103.

The first of these patients was a Muslim adult who had continuous pain around the umbilicus for three years. He had some anaemia and his general health had deteriorated. Treatment for chronic dysentery was ineffective. No parasites were found in the blood or stools other than *Giardia* cysts which were present on three consecutive daily examinations. Mepacrine in three courses at an interval of two weeks [dosage not stated] resulted in uninterrupted improvement.

The second patient was a child of seven with bronchial asthma, without eosinophilia. His liver was enlarged one inch below the costal margin. The general health was not affected. Treatment for asthma was ineffective. As the patient used to have one or two loose stools before the paroxysms of asthma, the stools were examined. *Giardia* cysts were numerous : there were no other parasites found in the stools or in the blood. A similar course of mepacrine was given : no attacks of asthma have occurred for several months and the enlargement of the liver has diminished. *H. J. O'D. Burke-Gaffney*

RITA, G. & LEVI DELLA VIDA, B. Coccidiosi umana da *Isospora.* (Su di un caso osservato a Roma.) [**A Case of Human Coccidiosis in Rome.**] *Riv. di Parassit.* Rome. 1949, June, v. 10, No. 2, 117–21, 3 figs. English summary (3 lines).

Infection of man by *Isospora belli* is not common ; the case reported here is only the fourth so far noted in Italy, previous ones being by SANGIORGI in 1918 [this *Bulletin*, 1919, v. 13, 22] and by FRANCHINI in 1927 [*ibid.*, 1928, v. 25, 726] and 1932. Infection is usually accompanied by some other parasite, protozoal or helminthic, and in the present instance by *Entamoeba histolytica* and *E. coli.*

The patient was an Englishman of 70 years, resident for three years in Rome. He suffered from gastro-intestinal disturbance with diarrhoea, and faecal examination revealed cysts and vegetative forms of *E. histolytica* and *E. coli*, and numerous oöcysts of coccidia. Treatment with emetine brought about improvement of the symptoms and disappearance of the entamoebae, but the coccidia could still be seen. It is difficult to say to what degree, if any, the symptoms were due to the *Isospora.* Attempts to infect four guineapigs and a monkey were not successful. The authors refer to the experimental infection of *Isospora hominis* in man reported in 1948 by MATSUBAYASHI and NOZAWA [see this *Bulletin*, 1949, v. 46, 261]. *H. Harold Scott*

HALAWANI, A. & EL KORDY, M. I. **The Incidence of Balantidiosis in Egypt with reference to the so-called Process of Budding in** *Balantidium coli.* *J. Roy. Egyptian Med. Ass.* 1948, Dec., v. 31, No. 12, 936–40, 1 fig.

According to previous records, human balantidiosis is very uncommon in Egypt. The present authors have re-investigated its incidence and have encountered only 3 cases in the course of the last 7 years. The examination of 20 specimens of stools of pigs slaughtered in the Cairo abattoir revealed *Balantidium* in 80 per cent. of the samples. They then turned their attention to pig-breeders in the suburbs of Cairo. The stools of 19 owners and members

of their families in one suburb were negative, while in another suburb a single case of infection with *Balantidium coli* was detected among 27 persons examined. The authors believe that " The rarity of balantidial infection in Egypt may be due to the fact that the great majority of Egyptians are Mahommedans who are not allowed to eat the meat of pigs, or to rear them ".

The authors have successfully grown *Balantidium coli* in a medium consisting of serum (human, equine, bovine or ovine) diluted with buffered Ringer's solution in the proportion of 1 : 10, with the addition of a small amount of rice starch.

Both in cultures and in natural infections they found a few ciliates producing bud-like outgrowths varying in size. Since these " buds " revealed no nuclei when examined in stained preparations they are not regarded as a form of multiplication of *Balantidium* and their nature remains doubtful. This condition of " budding " is shown in a photo-micrograph. *C. A. Hoare*

LEPROSY

LEPROSY IN INDIA. 1949, Apr., v. 21, No. 2, 39–121. **All-India Leprosy Workers' Conference, Calcutta, 29th to 31st December, 1948.**

This voluminous number contains little new information, as the views of the principal authors had been recorded in papers shortly before at the Cuba Conference. The table of contents lists the names and speeches of politicians and others, but not the medical papers, so every page has to be turned over to find the latter. Fortunately the few points of interest are summarized in Part II and include the following. The subject of treatment was opened by COCHRANE, who has made an advance on his former advice to limit the use of sulphones to the most experienced workers by going to the other extreme of pushing large doses without any intermission during reactions, except very severe ones, in all lepromatous cases, but he does not advise sulphones in neural macules, tuberculoid or neural anaesthetic lesions for fear of causing them to become lepromatous. DHARMENDRA is unable to understand this limitation. S. N. CHATTERJEE advises the injection of small doses such as 3·5 per cent. watery solutions of sulphetrone and diasone to a maximum of 5 cc., which produce clinical improvement without reactions or anaemia. These first two workers advise the combined use of sulphones and hydnocarpates [as advocated by the reviewer, see this *Bulletin*, 1948, v. 45, 614]. MUIR differed from Cochrane in finding sulphones useful in tuberculoid cases. TEICHMANN recorded the after-results of hydnocarpates in 105 cases, almost all lepromatous ones. Large doses gave the best results with 27·3 per cent. disease arrested for a time at least ; but results as a whole were poor, although definite reduction in the incidence of deformity occurred.

The control of leprosy was discussed on the second day without bringing out any important new points. The third subject for discussion was the histopathology and classification of leprosy. This brought out great differences of opinion and a tendency to ever-increasing complication of nomenclature.

L. Rogers

BLANCO, F. L. & FITE, G. L. **Silvering of Lepra Bacilli in Tissues.** *Arch. Pathology*. 1948, Dec., v. 46, No. 6, 542–9, 8 figs.

This is an important paper, which should be read in original by all interested in the bacteriology of leprosy and for the elaborate method used which takes

about five weeks to carry out. The organisms are stained black and brown with differences of intensity. In the most highly active lesions, parallel columns of bacilli radiate from the centre of the containing cell and are never in bundles as with fuchsin. These are abundant young growing bacilli. In the more common chronic lepromata the spaces in the vacuolated cells are free from organisms, which tend to curve round them and show a greatly diminished rate of multiplication. Many of the bacilli in old globi become progressively more weakly silvered especially those centrally placed: these are considered to be degenerated forms without change in morphology, which supports the idea that in old lesions death of the bacilli is constantly taking place. Pleomorphism of the lepra bacilli is only marked in chronic lesions. In silvered preparations clear narrow halos are seen around and separating the organisms. A new concept of the nature of the globus is thus offered. Good illustrations demonstrate the above points. *L. Rogers*

KAHN, R. L., BARIBEAU, Betty J. & VILLALON, Flora T. **Universal Serologic Reaction with Lipid Antigen. IV. In Lepromatous Leprosy.** *Amer. J. Clin. Path.* 1949, May, v. 19, No. 5, 408–13, 3 figs. [Summary appears also in *Bulletin of Hygiene.*]

Sera from 55 patients suffering from lepromatous leprosy were examined by the Universal Serologic technique, and typical results are shown in one table and three figures. Marked precipitation is noted before incubation and is strongest in the presence of reduced NaCl concentration; after 4 hours in the ice box almost all serum dilutions show precipitation, complete in zones I and III, nearly complete in zone II; after 24 hours' incubation all zones show complete precipitation. In contrast to the foregoing, in tuberculoid leprosy there was no difference in precipitation after 4 and 24 hours' incubation. It is suggested that in lepromatous leprosy there is not only an increase over the normal liberation of tissue lipoid but also liberation of distinctive lipoids; serological patterns vary with the activity of the disease, differing according as to whether it is active or "burnt-out"; these may serve to distinguish between different forms of the disease and as an index of response to treatment. *T. E. Osmond*

LASSMAN, P. Traitement de la lèpre humaine avec les produits extraits de graines des Oncobées du Congo Belge. [**Treatment of Leprosy with Extracts of Seeds of *Oncoba* from the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1949, Mar. 31, v. 29, No. 1, 23–8.

This brief note records a trial in the treatment of leprosy of an oil extracted from the seed of a species of *Oncoba*, such as that from *Caloncoba*, which was found by Dubois to be well tolerated in man [this *Bulletin*, 1942, v. 39, 857], and actively to inhibit the growth of avian tubercle bacilli in cultures, but whose chemical nature is unknown. Trials in cases, mainly lepromatous ones, by infiltration of the cutaneous lesions, including lepromata of the ears, and also intramuscularly in doses up to a total of 30 to 150 cc. per case, has resulted in clearing up of the skin lesions, and the method is equally effective in relapses. As no general reactions or toxic symptoms resulted further trials are indicated, although cures are not claimed. *L. Rogers*

STANCIOLI, J. & DINIZ, O. Primeiros resultados obtidos com a bogalita no tratamento de leprosos em Minas Gerais. [**First Records of the Results of Treatment of Leprosy in Minas Gerais with Bogalita.**] *Publicações Médicas.* São Paulo. 1948, Feb.–July, v. 19, No. 172, 19–29, 5 figs.

Bogalita, methanal [formaldehyde] sulphoxylate of sodium, has been tried in leprosy on the grounds that oxygen is necessary for growth of *Myco. leprae*

and that a reducing agent will interfere with that growth. The authors refer to the 12 cases reported by FERNANDEZ and BERGEL [see above] and then speak of 8 cases of their own, all patients in an advanced lepromatous stage, 5 from the Santa Isabel Colony and 3 from the Roça Grande Sanatorium. They gave the drug, first in glucose saline, later in distilled water [strength not stated, but Fernandez and Bergel gave it in 10 per cent. solution], starting with 1 gm. daily (except on Sundays) for a week, then 1 gm. night and morning, and increasing until in the fourth week 3·5 gm. were given twice a day, and this was kept up to the end of 8 weeks. As others have found, if it is injected too quickly nausea and vomiting might occur.

The results were : little or no change in the blood, no reduction of red cells, but usually some increase and maintenance of the haemoglobin value, the bacilli became fragmented and stained poorly, there was less nasal obstruction, less dysphonia, and improvement in the general health, with better appetite and sleeping. Lepromata softened and broke down. These changes are illustrated by photographs. [This drug is used also in leishmaniasis, see above, p. 926.] *H. Harold Scott,*

NOEL, R. & SOEUR MARIE-SUZANNE. Du mode de propagation du bacille de Stefansky inoculé dans la membrane chorio-allantoidienne de l'embryon de poulet. [**Development of Stefansky's Bacillus when inoculated on the Chorio-Allantoic Membrane of the Chick Embryo.**] *Ann. Inst. Pasteur.* 1949, June, v. 76, No. 6, 535–8, 3 figs.

GOMES, J. M. Ação do promin sôbre o Mycobacterium de Stefansky. Estudos morfológicos. **Morphological Study of the Action of Promin on Stefansky's Bacillus.** [*Arquivos Facul. de Hig. e Saude Pública Univ. de São Paulo.* 1948, June, v. 2, No. 1, 19–30. English summary. [13 refs.]

The author started with 36 rats which he divided into three groups : (1) Controls, inoculated with a suspension of triturated leproma tissue. (2) Similarly inoculated, but promin treatment started a month later and after 9 weeks' treatment there was allowed one week free and the promin was then resumed for another 2 months, the drug being used in a strength of 1 per cent. in milk. (3) As the last, but a month after resumption of treatment, the promin was stopped and carotenoid (1 cc. of a 0·1 per cent. colloidal suspension) injected three times each week. One month later, the carotenoid was suspended and promin again given for 10 days, after which all treatment was stopped. Some of the animals died but 16 lived for 4–6 months and were killed and examined. The controls showed a non-ulcerated leproma with bacilli, some smooth and short, others granular. The promin-treated animals (group 2), 6 in number, also showed a leproma locally in the right inguinal fossa ; in one apparently normal, one necrosed, two with ulcers cicatrizing and in two the leproma was regressing and fibrosed ; bacilli some long and smooth, others fragmented, some with dark granules and the organisms in globi. Those in group 3 showed fibrosed or ulcerated remnants of lepromata ; in only one were there bacillary globi, the majority were fragmented and granular.

It is thought that the carotenoid stimulates the vitality of the bacteria ; *In vitro* the colonies of acid-fast organisms grow more strongly, but *in vivo* an allergy is thus set up which results in destruction of the organism.

Summing up the changes briefly : In the controls there was leproma formation without any tendency to ulceration and the bacilli were generally smooth, short and granular. In those treated with promin alone lepromata were present,

but mostly retrogressing, long bacilli predominating and "resistant forms". Those treated with promin and carotenoid showed lepromata frankly retrogressed (in two they had gone altogether) and the bacilli were some long, some with dark granules and apparently degenerated forms.

H. Harold Scott

HELMINTHIASIS

NAGATY, H. F. **A Revised List of the Helminth Parasites of Man and Food Mammals in Egypt.** *J. Roy. Egyptian Med. Ass.* 1949, May, v. 32, No. 5, 423–5.

See also p. 976, COUDERT & JUTTIN, **A propos des méthodes d'enrichissement des selles.**

BARLOW, C. H. **A Theory of Egg-Deposition by** *Bilharzia haematobia.* *J. Parasitology.* 1949, Apr., v. 35, No. 2, 205–7.

A French version of this paper has already been abstracted [see this *Bulletin*, 1949, v. 46, 752].

STANDEN, O. D. **Experimental Schistosomiasis. I. The Culture of the Snail Vectors** *Planorbis boissyi* **and** *Bulinus truncatus.* *Ann. Trop. Med. & Parasit.* 1949, Apr., v. 43, No. 1, 13–22. [13 refs.]

The successful establishment of aquaria for the growth and breeding of snail vectors of schistosomes in localities far removed from their native environment, requires considerable care and attention to a variety of factors. In this paper the ecological requirements of the two important vectors, *P. boissyi* and *B. truncatus*, are described and discussed in relation to their culture in aquaria. Having outlined the habits of these two species, including feeding and reproduction, the optimum conditions of temperature, light, aeration and *p*H of the aquaria are stated. The results of trials with various species of water plants showed that the most suitable forms are *Vallisneria spiralis*, *Ludwigia palustris* and *Myriophyllum japonicum*, which, moreover, are easily obtainable. The merits of other water plants are offset by certain undesirable characteristics.

For the maintenance of these snails under biologically balanced conditions a study was made of the rôle of protozoa and a variety of aquatic invertebrates in the ecology of the snails. The harmful or beneficial actions of such forms as rotifers, oligochaets, crustaceans and molluscs have been observed and are discussed. Of the crustaceans, *Daphnia* plays an especially important part in controlling the numbers of unicellular organisms, and the oligochaets act as useful scavengers of vegetable débris. The significance of the multiplication of other organisms as indicators of the general health of the aquarium is commented upon.

Detailed instructions are given as to the procedure to be followed in setting up a balanced aquarium for snail culture and for its successful maintenance, together with useful hints as to the steps to be taken in the event of the appearance of signs of unbalance in the ecological environment.

J. J. C. Buckley

AZIM, M. A. & WATSON, J. M. **Comparative Efficiency of Different Methods of Packing the Snail Vectors of** *Schistosoma haematobium* **and** *S. mansoni* **for Transport by Air.** *Ann. Trop. Med. & Parasit.* 1949, Apr., v. 43, No. 1, 39–40.

Four well-known methods of packing snails were tested; in each case the snails were packed in wooden boxes, 15×25 cm., with perforated lids. The

methods were (1) a layer of fine silver-sand, wetted to a paste, about 1 cm. thick on the bottom of the box : the snails were placed on this and a similar layer of wet sand placed on top of them ; (2) as (1), with finely ground wood charcoal instead of sand ; (3) open-ended tubes, 15 cm. long and 2 cm. in diameter, containing alternate layers of snails and wet dead leaves ; the full tubes were covered with a double layer of fine-mesh gauze sealed in position with tape. The boxes containing the tubes were packed with more wet dead leaves ; (4) a layer of wet pond-mud, about 1 cm. thick on the bottom of the box, with the snails on top of it and the rest of the space in the box filled with water-weed. This last is the method used for despatch abroad of snails from the Bilharzia Snail Destruction Section, Ministry of Public Health, Cairo.

The snails used were *Planorbis boissyi* and *Bulinus truncatus*.

All four boxes were placed in the shade for 72 hours (maximum daily shade temperature, 115°, 96° and 99°F.).

After unpacking, the sand was very dry, the charcoal had caked, the leaves, mud and water-weed were quite moist.

The snails were removed under water, cleaned in running water at 27°C. in a net and observed in aquaria for 24 hours. In the case of *P. boissyi*, the percentages of survivors in mud, sand, leaves and charcoal respectively were 97, 95, 94·5 and 90 ; corresponding figures for *B. truncatus* were 23·2, 2·0, 1·0, 11·0.

It is evident that packing in damp mud, in perforated wooden boxes with adequate air-space and covered with moist water plants was the most satisfactory. The results were borne out in the case of actual consignments sent abroad from Cairo (*e.g.* to Britain and to the U.S.A.).

Brief reference is made to other methods of packing for other species of snails.

H. J. O'D. Burke-Gaffney

DESA, A. E. & MONTEIRO, L. **Urinary Schistosomiasis in India with a Report of One Case.** *Indian J. Med. Sci.* 1949, June, v. 3, No. 6, 376–81, 2 figs. on pl. [16 refs.]

Reference is also made to 9 previous cases in India.

ALVES, W. **Miracil D in Urinary Bilharziasis.** *South African Med. J.* 1949, May 28, v. 23, No. 22, 428–31.

BLAIR *et al.* [this *Bulletin*, 1949, v. 46, 556] have shown that urinary schistosomiasis can be cured by a 5-day course of miracil D totalling 75–100 mgm. per kgm. In the present work, smaller doses were tried, *viz.* :—

(1) Sixty mgm. per kgm. given in six divided doses, twice daily for three days. Twenty young Africans were treated ; nine complained of side effects such as nausea, headache or dizziness but there were no major disturbances. Four weeks later, no living eggs were being passed in the urine and all twenty patients are considered cured.

(2) Sixty mgm. per kgm. given in four divided doses in four days to twenty young Africans. Only five complained of minor symptoms. Four weeks later, three of them were still passing occasional live eggs. Seventeen are considered cured.

(3) Seventy-five mgm. per kgm. in ten divided doses during five days, given to thirty-five young Africans. Nine had minor toxic effects. After four weeks all are apparently cured.

It is believed that patients who have not relapsed in four weeks are unlikely to relapse. "Miracil D appears to be a relatively non-toxic drug but it is extremely unpleasant to take and is definitely a gastro-intestinal irritant".

The subjects of these studies were schoolboys under discipline ; and patients in the Native Reserves might be less ready to take the treatment. But Miracil is strongly recommended for all cases where control can be exercised.

F. Hawking

MOORE, D. V., YOLLES, T. K. & MELENEY, H. E. **A Comparison of Common Laboratory Animals as Experimental Hosts for** *Schistosoma mansoni*. *J. Parasitology*. 1949, Apr., v. 35, No. 2, 156–70, 1 fig.

"The common laboratory animals (mice, hamsters, rats, guinea pigs and rabbits) were infected with *S. mansoni* by two methods : intraperitoneal injection and cutaneous exposure. The course of the resulting infection was studied and the following points used as a basis for comparing the suitability of the animals as hosts for *S. mansoni* : percentage worm recovery, time required for the worms to reach maturity, and the presence of viable eggs in the feces.

"1. *Mice*. Animals infected with 100 cercariae yielded an average of 21·4 per cent. worm recovery following intraperitoneal infection and 22·9 per cent. following percutaneous infection. Eight weeks after infection 96–99 per cent. of the worms were mature. Viable eggs appeared in the feces 6–6½ weeks after infection and egg passage continued until the death of the animals.

"2. *Hamsters*. Animals infected with 160 cercariae yielded an average of 17·9 per cent. worm recovery after intraperitoneal infection, 18·1 per cent. after unshaved percutaneous infection, and 29·2 per cent. after shaved percutaneous infection. Eight weeks after infection 89–97 per cent. of the worms were mature. Viable eggs appeared in the stool 5–6 weeks after infection and egg passage continued until the death of the animals.

"3. *Rats*. Animals infected with 100–6,000 cercariae yielded an average of 0·9 per cent. worm recovery following intraperitoneal infection and 2·3 per cent. after percutaneous infection. Ten weeks after infection 67–89 per cent. of the worms were mature, but were smaller than in mice and hamsters. Eggs were never demonstrated in the feces at any time.

"4. *Guinea Pigs*. Animals infected with 500–2,000 cercariae yielded an average of 0·5 per cent. worm recovery following intraperitoneal infection and 22·9 per cent. after shaved percutaneous infection. Eight weeks after infection 82 per cent. of the worms were mature, but were smaller than in mice and hamsters. Eggs were never demonstrated in the feces at any time.

"5. *Rabbits*. Animals infected with 500–15,000 cercariae yielded an average of 0·3 per cent. worm recovery following intraperitoneal infection and 11·8 per cent. after percutaneous infection. Seven to 8 weeks after infection 63–67 per cent. of the worms were mature, but were smaller than in mice and hamsters. Eggs were never demonstrated in the feces at any time.

"6. It is concluded that mice and hamsters are the most suitable common laboratory animals for experimental infections with *S. mansoni*. Rats are unsatisfactory hosts because very few worms develop to maturity. Guinea pigs and rabbits are of value only for producing large numbers of worms, and must be infected by percutaneous exposure."

WATSON, J. M. & AZIM, M. A. **Comparative Efficiency of various Methods of infecting Mice with** *Schistosoma mansoni*. *Ann. Trop. Med. & Parasit.* 1949, Apr., v. 43, No. 1, 41–6.

The authors exposed mice to infection with cercariae of *S. mansoni* by eight different methods, with the object of evaluating their relative efficiency. The technique employed in each method is described and it was concluded from the results that the partial-immersion method ranks first, provided that precautions

are taken against contamination of the water by urine and faeces of the mice, which are lethal to the cercariae. The cover-slip method ranks next in reliability but has the disadvantage of taking up much time and only allows a limited application of cercariae. The tube method and oral method were also successful but less constant in results than the previous methods. Inoculation by vaseline ring, subcutaneous injection and intraperitoneal injection all gave relatively poor results. There was complete failure by the gastric-injection method.

J. J. C. Buckley

HITCHCOCK, Dorothy J. **Penetration Characteristics of** *Schistosoma mansoni* **Cercariae.** [Research Notes.] *J. Parasitology.* 1949, Apr., v. 35, No. 2, 216–17.

To estimate the time taken for the penetration of skin by a schistosome cercaria, the process was observed under a magnification of 40× and strong illumination, with the use of cercariae of *S. mansoni* applied to hamsters. The average time for penetration, measured from the time of placing the cercariae on the skin to the time of their disappearance below the surface, was 4·3 minutes for the 75 cercariae observed, the range being 2 to 15 minutes. With the use of mice instead of hamsters, the average time for 50 cercariae was 3·6 minutes, with a range of 2·5 to 8 minutes. When placed on the skin, in a drop of water, the cercariae usually swam around for one minute and then crawled by means of the oral sucker. During penetration they were attached to the skin by the oral sucker, the body being perpendicular. The tail was in violent movement but only broke from the body when the latter had completely penetrated. [From the description, it might reasonably be inferred that the cercariae penetrated the skin when fully submerged and without the aid of an evaporating film of water. (See also OLIVIER, this *Bulletin*, 1949, v. 46, 849).]

J. J. C. Buckley

MEIRA, J. A. & SOARES, J. C. M., Jr. A biopsia retal no diagnóstico da esquistosomíase mansoni. [**Diagnosis of Schistosomiasis mansoni by Rectal Biopsy.**] *Arquivos Facul. de Hig. e Saude Pública Univ. de São Paulo.* 1948, June, v. 2, No. 1, 45–90, 9 figs. on 5 pls. [24 refs.] English summary.

The authors, after referring to previous reports on the results of rectal biopsy examination in cases of *S. mansoni* infestation, record their own results in 42 cases in which 53 such biopsies were made. They refer in some detail to the findings of HERNANDEZ-MORALES & MALDONADO who, in 1946, reported on 138 patients 50 of whom had had no treatment, while 88 had been given antimonials. Of the former all were positive by rectal biopsy, although less than half [the authors state 41·6 per cent., presumably 21 of the 50, but why not 42 per cent.?] were positive by faecal examination. Of the 88 who had had antimony treatment 70·3 per cent. [62 patients] were positive by rectal biopsy, whereas faecal examination diagnosed only 16 (18·2 per cent.). Moreover, for the untreated patients an average of 3·3 faecal examinations were needed before a positive finding was obtained and 10 were needed for those treated [see this *Bulletin*, 1947, v. 44, 330]. The authors then detail the results in their own cases, in which rectal biopsy and faecal examination were both made, the one to check the other. Sometimes repeated faecal examination proved negative (in one case as many as 14) although biopsy was positive. All had been sent in as suspicious of *mansoni* infection. Seventeen were positive by biopsy and 25 were negative, and though among the former examination of faeces might be persistently negative, in none of the latter were faeces positive and biopsy

negative. [They state that biopsy specimens may be taken repeatedly without inconvenience or mishap, but in one patient there was such profuse haemorrhage that blood-transfusion was called for, and as regards the inconvenience the evidence of the patient might not coincide with that of the authors and should certainly have more weight.] *H. Harold Scott*

INGALLS, J. W., Jr., HUNTER, G. W., MCMULLEN, D. B. & BAUMAN, P. M. **The Molluscan Intermediate Host and Schistosomiasis japonica. I. Observations on the Conditions governing the Hatching of the Eggs of** *Schistosoma japonicum.* *J. Parasitology.* 1949, Apr., v. 35, No. 2, 147–51.

"The results from studies of environmental conditions which might be expected to influence the hatching of *S. japonicum* eggs indicated there is no effect on the rate of hatching as a result of the degree of intensity of illumination, agitation of fecal matter in the suspension, or osmotic stimuli. No diurnal or nocturnal cyclic frequency in hatching rates was observed. A temperature range of 25°C. to 30°C. was found satisfactory. The work indicated that to obtain consistently good results it is most important that the fecal material be thoroughly washed and the water in the hatching flasks be clean and alkaline. The best miracidial yields were secured in water with *p*H 7·6. After hatching ceased in a flask, it was possible to obtain second and third yields by re-sedimenting the fecal material."

YOKOGAWA, S. & RO, M. **Studies on the Treatment of Paragonimiasis. Part III. Histo-pathological Changes in the Foci of Lungs, and in Flukes of Dogs experimentally treated.** *Acta Nipponica Med. Trop.* Taihoku. 1942, Aug., v. 4, Nos. 1/2, 1–58, 24 figs. on 4 pls. [10 refs.]

[See this *Bulletin*, 1941, v. 38, 47.]

LEIPER, J. W. G. **Continuous Sedimentation for the Concentration of Trematode Eggs in Faecal Suspensions.** [Correspondence.] *Nature.* 1949, June 11, 908, 1 fig.

An apparatus for concentrating trematode eggs is described which has the advantage of rapidly reducing the faecal débris to less than half and of washing away colouring matter with the loss of only very few eggs. It is specially adapted for use with sheep faeces which have a high proportion of débris and it has proved of value in recovering eggs of *Fasciola hepatica* and *Paramphistomum cervi*. It consists of a U-tube having a funnel at the end of one upright arm and a spherical flask 4·5 cm. [shown in list as 4·5 mm.] in diameter at the other, from which liquid can be siphoned off. The apparatus is filled with water, except for an air lock in the spherical flask ("distillation splash head"), and the faecal suspension, having first been passed through a sieve of 40-meshes per inch, is placed in the funnel. The siphon is then opened and the suspension passes through, but eggs and heavier particles settle at the bottom of the U-tube, from which they are recovered. *J. J. Buckley*

HARANT, H. & MIDROUILLET, Mme. Sur un nouveau cas de coenurose humaine. [**A New Human Case of Coenurosis.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 5/6, 173–4.

The authors refer to the rarity of human infection by *Coenurus* and quote some of the few proved cases in the literature [this *Bulletin*, 1920, v. 15, 223; 1932, v. 29, 54 and 416; 1934, v. 31, 120 and 787; 1942, v. 39, 631 and 872; also 1949, v. 46, 65 and 561].

They then give a brief account of a case in a peasant from the Department of Tarn. The patient was a deaf-mute and during a routine medical examination, a cyst about the size of a pigeon's egg was found in the left deltoid region. Operation showed that the cyst was partly embedded in the deltoid muscle and its wall was closely associated with the fibres. The cyst burst during surgical intervention, releasing a clear fluid : the cavity contained about 10 to 20 whitish granulations about the size of a pin's head. Microscopic examination revealed the presence of a coenurus which was identified as that of *Multiceps serialis.*

H. J. O'D. Burke-Gaffney

COUTELEN, F., COCHET, G. & BIGUET, J. Présence d'*Hymenolepis nana* dans le Nord de la France. [*Hymenolepis nana* **in the North of France.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 3/4, 106–11. [18 refs.]

Six cases of *Hymenolepis nana* infection were recorded in the North of France in 1948 and all were autochthonous. Three were in a community of children, two were in one family and the sixth was an isolated case. Epidemiological investigation suggested a possible explanation of these infections.

H. J. O'D. Burke-Gaffney

NEGHME R., A., FAIGUENBAUM A., J., PILOTTI A., M. & SILVA CAMPOS, R. Algunos aspectos epidemiológicos de la hidatidosis humana en Chile. [**Some Epidemiological Aspects of Human Hydatidosis in Chile.**] *Bol. Oficina Sanitaria Panamericana.* 1949, May, v. 28, No. 5, 469–77, 2 graphs.

The English summary appended to the paper is as follows :—

" From a study made of some of the epidemiological aspects of hydatidosis in Chile during a period of 12 years (1933–1945), the authors arrived at the following conclusions : the incidence of hydatidosis in Chile is low in relation to other common infections, though it must be said that during recent years the epidemiological curve has gone up ; as to its geographical distribution, in varying degrees of intensity, it has spread throughout the country ; although the disease has no special preference as regards sex, it occurs slightly more frequently in men ; it is unknown in nursing children ; the incidence is low in children under 10 years and in persons over 60 years old ; and 90 per cent. of the cases are found in persons from 11 to 59 years of age ; the over-all death rate for this disease in Chile remains stationary although the death rate for the total number of persons affected with the disease has risen during recent years."

JOYEUX, C. & BAER, J. G. L'hôte normal de *Raillietina* (*R.*) *demerariensis* (Daniels, 1895) en Guyane hollandaise. [**The Normal Host of** *Raillietina* (*R.*) *demerariensis* **in Netherlands Guiana.**] *Acta Tropica.* Basle. 1949, v. 6, No. 2, 141–4.

Two cestode strobilae which had been collected from a howler monkey, *Alouatta seneculus*, in Surinam, were identified as *Raillietina* (*R.*) *demerariensis*, a species which has hitherto been recorded only from man. The material is described in detail and the chief morphological characters of this species and of *R. alouattae* Baylis, 1947, which it closely resembles, are tabulated.

R. alouattae also occurs in the howler monkey, *Alouatta maconnelli.* The howler monkey is thus established as the normal host of two species of *Raillietina*, one of which is capable of infecting human beings.

J. J. C. Buckley

BAER, J. G., KOURÍ, P. & SOTOLONGO, F. Anatomie, position systématique et épidémiologie de *Inermicapsifer cubensis* (Kourí, 1938) Kourí 1940, cestode parasite de l'homme à Cuba. [**Anatomy, Systematic Position and Epidemiology of** *Inermicapsifer cubensis* **(Kouri, 1938) Kouri 1940, Cestode Parasite of Man in Cuba.**] *Acta Tropica*. Basle. 1949, v. 6, No. 2, 120–30, 14 figs. [15 refs.]

"A detailed anatomical study of *Inermicapsifer cubensis*, based on the original material deposited in the School of Tropical Medicine in Havana, shows that we are dealing with a single, well defined species of this genus.

"Over one hundred cases have been recorded so far from the western parts of the island. It is very likely, however, that this parasite will be found in other parts of Cuba as well as in Porto-Rico and Venezuela.

"Children of the age 1–5 years and 9–11 years are most frequently infested. All cases except two have been recorded from white children.

"It is probable that parasitism is accidental and that the normal host will be found amongst the Cuban fauna. No systematic research has been made so far with this end in view. Among native rodents, "Jutía s" (*Capromys pilorides* and *C. prehensilis*) apparently do not harbour this worm.

"Inermicapsiferiasis is discovered by finding the ripe segments, singly, in the feces. These cannot, however, be distinguished from those of *Raillietina*, the presence of which, in the West Indies, is quite possible. It is always necessary to recover the scolex and to examine it for the presence of the peculiar hooks of this genus."

BAYLIS, H. A. **A New Human Cestode Infection in Kenya.** *Inermicapsifer arvicanthidis*, **a Parasite of Rats.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, May, v. 42, No. 6, 531–42, 5 figs. [22 refs.]

Two strobilae of *Inermicapsifer arvicanthidis* (Kofend, 1917) were evacuated, after anthelmintic treatment, by a boy aged two from Kenya who had been passing tapeworm segments. The boy had lived in Nairobi until April 1948 when he came to England and some weeks later was admitted to hospital. The vermifuge employed was filix mas, minims 15, given with jam and honey in the evening and retained during the night. Early next morning, syrup of figs, drachm 1 was given and the tapeworms were recovered in the stool.

In the fresh condition these measured about 25 cm. and after preservation were about 17·9 cm. and 18·5 cm. respectively with a maximum width of 3 mm. The segments numbered about 315 and 360 and, except for the terminal segments, were broader than long. As the species is new to medical literature the author gives a detailed and complete description of it, based on this human material and a specimen from a rodent host. A hitherto unmentioned feature was noted in the excretory system, in which the ventral longitudinal vessels were seen to be 4 to 6 in number and to be interconnected by a network of transverse vessels.

This species has been recorded from rodent hosts in various parts of Africa; in the Sudan, from *Arvicanthus niloticus kordofanensis*; in Dahomey, from *Arvicanthus niloticus rufinus* and ? *Oenomys hypoxanthus*; in Nigeria, from *Hybomys univittatus*, *Lemniscomys striatus*, *Tatera kempi* and *Rattus* (*Mastomys*) *coucha erythroleucus*; in French Guinea, from *Pelomys* (*Golunda*) *campanae*; in Tanganyika, from *Rattus* (*Mastomys*) *coucha microdon* and *Heliophobius argenteocinereus emini*; in the Belgian Congo, from *Rattus* (*Mastomys*) *coucha* (subsp. ?); in Southern Rhodesia, from *Steatomys pratensis*; in S. Africa, from *Thallomys* (*Mus*) *moggi* and *Otomys irroratus*. Although

I. arvicanthidis has yet to be recorded from rodents in Kenya, it is considered that its present occurrence in a human host represents an occasional or accidental infection.

With the interesting exception of *I. cubensis* (Kouri, 1938) recorded from human beings in Cuba [see this *Bulletin*, 1941, v. 38, 113] *Inermicapsifer* appears to be an African genus and the suggestion is made that the Cuban species may have been introduced from West Africa. Moreover, the possibility exists that *I. cubensis* and *I. arvicanthidis* may be identical, as the author's comparison of the two species seems to indicate.

The life-cycle of *Inermicapsifer* is unknown, but in other members of the Anoplocephalidae, in which this genus is placed, the intermediate hosts have been found to be mites. However, it is suggested that the vector of *Inermicapsifer* is more likely to be an insect, as its egg capsules appear too large to be swallowed by mites. The close resemblance of the egg capsules to those of *Raillietina*, of the family Davaineidae, certain species of which are transmitted by beetles and ants, supports the idea of an insect intermediary for *Inermicapsifer*; and if this should be confirmed by future researches, it would further establish the resemblance between the two genera and lead to a reconsideration of the present classification of *Inermicapsifer*.

J. J. C. Buckley

PATEL, J. C. **Ankylostomiasis as it faces the Practitioner.** *Indian J. Med. Sci.* 1949, May, v. 3, No. 5, 339–48. [11 refs.]

A general discussion and review.

BEAVER, P. C. **Quantitative Hookworm Diagnosis by Direct Smear.** *J. Parasitology.* 1949, Apr., v. 35, No. 2, 125–35, 3 figs. [11 refs.]

The use of direct faecal smears in egg-counting for an approximate estimation of hookworm burden, is dependent on the assumption that the eggs are uniformly distributed in the faecal mass, and its value is impaired by the fact that faecal smears vary in volume and do not represent a uniform sample of faeces. The author devised a method of standardizing faecal smears and then applied it to determining the reliability of egg-counts of standard smears as compared with the Stoll dilution egg-count method.

To standardize direct smears, they are brought to a uniform standard density by means of a photo-electric foot-candle meter. A drop of water is placed on a slide and a small portion of faeces is mixed into it until an even density is obtained. It is then spread to a diameter of 16 mm. and the slide is placed on the meter over an aperture of 16 mm. diameter. Vertically above there is an electric lamp (75–100 watts) adjusted to give a reading of about 20 foot candles when a clean slide is placed over the aperture. Faeces are then added to the smear until the light is reduced to exactly 10 foot-candles. All forms of gross débris are removed from the smear before it is made up to the standard density. The eggs are then counted in the smear after it is covered with a coverglass.

Counts were carried out on stools from 10 different persons by this method (standard direct smear) and by a dilution method. Ten successive counts were made on each stool by each method. In another series five successive counts were made on 41 stools. Comparison of the two methods showed that they are about equally variable, the average of the coefficients of variation being 21 and 20 respectively in the first series and 22 and 25 in the second. The relationship between the number of eggs per slide and the number of eggs per cc. of stool was also examined and a close correlation was found between the two methods. With the use of a conversion factor of 300, standard direct smear counts can be

interpreted approximately in terms of number of eggs per cc. on a formed-stool basis. Periodic egg-counts on stools from the same person gave results as uniform by standard direct smear as by dilution methods.

Investigation of the relationship between egg-counts and hookworm burden was carried out by egg-counts made by both methods, followed by worm counts after treatment with tetrachlorethylene. From the results obtained it was concluded tentatively that each egg by standard smear count represents roughly 10 mature worms. *J. J. C. Buckley*

CRUZ, J. R., GUYTINGCO, A. & KASILAG, Wilhelmina R. **Observations on Hookworm Anemia in the North General Hospital.** *J. Philippine Med. Ass.* 1949, Apr., v. 25, No. 4, 191–4.

Hookworm anaemia has become much more prevalent than before in Manila during the last year, 1947–1948. The authors attribute this to the Japanese occupation, but note that the widespread increase in hookworm infection took several years to produce an increase in cases of hookworm anaemia ; another factor is the present-day relative rarity of anaemia due to malaria and malnutrition.

The anaemia was usually of the hypochromic microcytic type, but in 2 cases it was hypochromic macrocytic and in three hypoplastic or aplastic. Two patients with aplastic anaemia died ; there was one other death in the series.

About 60 per cent. of 42 cases in this series were diagnosed at the first stool examination and about 14 per cent. required 3 to 7 examinations before ova were found.

Most of the patients required 2 or 3 courses and 3 required 4 courses of either hexylresorcinol crystoids, 1·0 to 1·4 grammes, or tetrachlorethylene, 3 ml., at intervals of 6 days ; despite these repeated courses, 15 of the 42 patients were discharged with ova in the stools. *L. E. Napier*

BRAUN-BLANQUET, M. A propos de l'activité de l'essence de *Chenopodium ambrosioides.* [**On the Activity of the Oil of** *Chenopodium ambrosioides.*] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 3/4, 116–18.

The French preparation, oil of *Chenopodium ambrosioides* locally grown in Montpellier, which has an ascaridol content of 60 to 80 per cent., was given to several patients with nematode infections in the doses usually prescribed for the American preparation, namely, 1·0 to 1·5 ml. for an adult, divided into three doses, given in the morning on an empty stomach at intervals of an hour, followed one and a half hours after the last dose by 30 to 40 grammes of sodium sulphate. For ankylostomes this is often repeated several times at intervals of not less than 10 days.

This dosage was given to 30 patients and was well tolerated except in one cardiac case. In one case of *Trichocephalus* infection there was a clinical and parasitological cure and in another a reduction in the number of eggs in the faeces.

Nine patients with ankylostomiasis were treated. Sometimes as many as 100 adult worms were passed within 48 hours. In all there was improvement in the symptoms and sometimes in the blood picture. In seven cases there was a clinical and parasitological cure, the latter being confirmed by at least two stool examinations.

The best results were obtained with *Ascaris* infections. Nineteen patients were given a single treatment of 1·0 to 1·5 ml. ; all were completely freed of the parasites, the results being controlled by at least two stool examinations.

The author concludes that the French oil of chenopodium is as effective as that imported from the United States before the war and now unobtainable in France. [This is the therapeutic trial with the locally manufactured oil referred to in this *Bulletin*, 1947, v. 44, 1013 (HARANT, *et al.*).] *L. E. Napier*

BRANNON, Mary J. C. & FAUST, E. C. **Preparation and Testing of a Specific Antigen for Diagnosis of Human Strongyloidiasis.** *Amer. J. Trop. Med.* 1949, Mar., v. 29, No. 2, 229–39.

"A test antigen prepared from clean filariform larvae of *Strongyloides* cultured from the feces of the chimpanzee and extracted in isotonic (0·425 per cent) salt solution or Coca's solution, in dilution 1 : 100 produced 23 positive intradermal reactions and 25 positive precipitin tests in 25 chronic cases of human strongyloidiasis. Additionally there were two doubtful intradermal reactions, one in a moribund patient and one in a patient who had very severe exfoliative dermatitis. The precipitin titers ranged from 1 : 5,000 to 1 : 30,000. This antigen produced consistently negative, doubtful or weak intradermal and precipitin tests in 105 of 108 presumably uninfected control cases.

"The diagnostic significance of the positive intradermal and precipitin reactions has been demonstrated in these cases of *Strongyloides* infection. The tests provide a reliable index of infection. In cases of presumably cured *Strongyloides* infection the value of the intradermal and precipitin test is not so clear. It is not known how long after cure the intradermal reaction will remain positive, although it is likely that the precipitin test as carried out indicates the presence of specific antibodies."

LIE KIAN JOE. **Helminthiasis of the Intestinal Wall caused by** *Oesophagostomum apiostomum* **(Willach, 1891) Railliet and Henry, 1905.** *Documenta Neerlandica et Indonesica de Morbis Tropicis.* Amsterdam. 1949, Mar., v. 1, No. 1, 75–80, 3 figs. [12 refs.]

Eight nodules were found at autopsy in the submucosa of the caecum and ascending colon of an Indonesian male, aged 45 years. The nodules were 7 mm. to 10 mm. in diameter, semi-globular in shape and inconspicuous, and when they were opened a living nematode was found in each of six of the nodules. Two nodules which were perforated were empty, but a dead female worm was found in the lumen of the intestine. Of the 7 worms, 4 were males and 3 were females. Histologically the nodules showed a wide cavity deep in the mucosa, surrounded by necrotic material and a thin layer of connective tissue, containing lymphocytes, plasma cells, other round cells and a few neutrophile leucocytes. The necrotic layer tends to liquefy and it is assumed that the worm produces substances that dissolve the cyst wall.

The worms are identified as *Oesophagostomum apiostomum* and a detailed description of their morphology is given and illustrated. *J. J. C. Buckley*

OCHSNER, A., DEBAKEY, E. G. & DIXON, J. L. **Complications of Ascariasis requiring Surgical Treatment. Report of Case with Abdominothoracic Complications.** *Amer. J. Dis. Children.* 1949, Mar., v. 77, No. 3, 389–407, 10 figs. [Refs. in footnotes.]

Complications of ascariasis requiring surgical intervention have been frequently recorded in the literature. Since they are usually of a serious nature and offer a rather poor prognosis, it is imperative that the diagnosis be made early and treatment be promptly instituted. The types of lesion produced include mechanical obstruction produced by the adult worms and bacterial

contamination transmitted by its migratory habits. Since ascariasis is commoner in children, a higher incidence of surgical complications would be expected in them, but they are not infrequently encountered in adults. Ascarides may produce mechanical obstruction in any hollow organ, such as the trachea, intestine, bile or pancreatic ducts and others. Intestinal obstruction from a bolus of entangled worms most commonly occurs in the lower ileum. Intussusception and volvulus may result from the irritation caused by the presence of one or more worms which do not necessarily obliterate the intestinal lumen. Ulceration and perforation of the small or large intestine may occur, with migration of the worms into the peritoneal cavity. It is not uncommon to find ascarides in a suppurating or gangrenous appendix ; of 1,000 surgically removed appendices in a New Orleans hospital, ova of *A. lumbricoides* were found in the faecal contents of 46. Migration of the parasite into the bile or pancreatic ducts, leading to suppurative or haemorrhagic pancreatitis, has been frequently reported. Multiple hepatic abscesses, which may rupture into the peritoneal cavity or thorax, are occasionally met with. The migrating larvae may cause bronchopneumonia, as was demonstrated by the Japanese brothers Koino in 1922 [this *Bulletin*, 1923, v. 20, 235] by experiments on themselves, and larvae and ova have been recovered from the sputum in cases of pulmonary infection, which may proceed to empyema and abscess formation.

Diagnosis depends on recovering the ova from the stools, or larvae or worms from the involved organ. A history of vomiting or passing worms is important and blood examination usually reveals anaemia and eosinophilia. An X-ray examination after a barium meal may show shadows due to the ingestion of barium sulphate by the ascarides. As a rule however the diagnosis is rarely made before operation. The authors prefer hexylresorcinol as the anthelmintic before operation, but warn against too vigorous employment of purgatives, which may produce intestinal obstruction. At operation enterotomy and evacuation of the bolus is the only safe method, but the length of bowel involved may be so great that this is not practicable ; in such cases a temporary ileostomy may be performed. Intussusception and volvulus are best corrected without enterotomy, though gangrene may necessitate resection. The treatment of perforation, general peritonitis or local abscess is on the usual surgical lines. Invasion of the gall bladder calls for cholecystectomy and in all such cases the common bile duct should be explored and drained. Hepatic abscesses are usually multiple and are treated by evacuation of the worms and drainage after packing off neighbouring organs.

The authors conclude with an account of a case of multiple hepatic abscesses in a child aged 20 months, in whom after the evacuation of an abscess in the right lobe of the liver which contained 24 worms, a similar mass was discovered high up on the dome of the right lobe too inaccessible to be dealt with at the time. This subsequently perforated the diaphragm and infected the thorax and the patient did not survive thoracotomy ; at autopsy no worms were found in the cavity in the liver nor any in the intestinal tract.

A large number of references are summarized in this paper and there are several good illustrations.

[A review of this subject by H. Milwidsky was summarized in this *Bulletin*, 1946, v. 43, 568.] *W. L. Harnett*

Woodman, H. M. **Filaria in the Anglo-Egyptian Sudan.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, May, v. 42, No. 6, 543–58, 1 map, 1 text fig. & 4 pls. [52 refs.]

Except for a small focus of *Wuchereria bancrofti* in the Nuba Mountains, filariasis is confined to the two southernmost provinces of the Sudan, Equatoria

and Bahr el Ghazal. Microfilariae only of *W. bancrofti* have been found infrequently ; no clinical cases have been diagnosed there recently.

Loa loa infection is found from 6°N. down well into the Belgian Congo and from French Equatorial Africa to 30°E. About 20 per cent. of the native population are affected. " Its only proved vector is *Chrysops distinctipennis* and *C. longicornis*, which occur in the ratio 26 : 1." Its development in these species is much slower than that described by CONNAL and CONNAL [this *Bulletin*, 1922, v. 19, 654] for *C. silacea* and *C. dimidiata*. Of 600 wild flies dissected, 0·6 per cent. showed embryos of *L. loa* [*sic.* ? 3 or 4 flies]. The author considers that these are probably not the main vectors in the Sudan. Other vectors are considered. In a species of *Haematopota* fed on an infected man some development occurred.

Acanthocheilonema perstans is found in 50 per cent. of the native population in these southern provinces of the Sudan. *Culicoides grahami* is presumably the vector.

The hyperendemic area for *Onchocerca volvulus* lies between French Equatorial Africa and 30°E., and between 6°N. and 9°N. South of this area occasional nodules due to this parasite are seen, but blindness is rare. Two surveys were made at points on the Sue river, at approximately latitudes 5°N. and 6°N. ; in the former 50 per cent. of persons selected (with nodules or other suggestive signs) showed microfilariae in their skins and in the latter 88 per cent. In the latter area 77 per cent. of the apparently healthy population showed microfilariae ; of 1,440 people in all, the precentage with nodules was 3·1 and with blindness was 0·48. The blindness did not all appear to be due to *O. volvulus*.

Antigen made from avian filariae was used for intradermal tests : 91·7 per cent. of cases gave a positive result and 5 a weak positive [the nature of the cases is not stated]. *L. E. Napier*

WANSON, M. Essai de traitement curatif de la filariose à *Loa-loa* et de la filariose apériodique par les dérivés de la pipérazine. [**Therapeutic Trial of Piperazine Derivatives in Loiasis and Aperiodic Filariasis.**] *Ann. Soc. Belge de Méd. Trop.* 1949, Mar. 31, v. 29, No. 1, 73–80.

In his main series, the author treated 10 Europeans and 36 Africans with hetrazan. In some subjects (not included in his main series) who did not take the full course of hetrazan, it was found that doses of 0·5–1·25 mgm. per kgm. three times daily for 10–21 days were ineffective and the number of microfilariae was unchanged.

In the cases of infection with *Loa* alone, the Europeans showed the usual symptoms, especially eosinophilia and prurigo. The 15 African patients were mostly without symptoms but in 4 of them (in whom the blood contained 500–800 microfilariae per 20 mm^3) there was emaciation. Twenty-one of the African patients harboured both *Loa* and *A. perstans*.

The dosage was 2 mgm. of base per kgm. thrice daily for 10 days by mouth. This was well tolerated, even by the 4 heavily infected Africans. *Mf. loa* disappeared rapidly from the blood within 48 hours.

Many of the Europeans complained of subcutaneous sensations resembling those caused by movements of the worms. There was also a transitory recrudescence of prurigo and other symptoms. After 48 hours, these symptoms gradually disappeared, the prurigo being the last to go. In 5 out of 10 cases, the apparent cure has lasted 3 months. But usually in both races the symptoms return after 4–12 weeks and the patients request further treatment. Accordingly the author recommends courses of 15 or 21 days, repeated 2 to 5 times at intervals of one month. Such courses have led to great and prolonged clinical

improvement but it is premature to claim radical cure. Hetrazan is not effective against *Ascaris*, *Strongyloides*, *Trichuris* or *Ancylostoma* [but see this *Bulletin*, 1949, v. 46, 385, where OLIVER-GONZALEZ *et al.* claim that all worms [*Ascaris*] were apparently removed from 3 of 6 patients after hetrazan]. Doses of 450 mgm. per day for 15 days have had no effect on *A. perstans*. *F. Hawking*

LAGRANGE, E. Essais de traitement des filarioses à *Loa-loa* et *O. volvulus* par le diéthylcarbamazine Chl. [**Treatment of Filariasis due to** *Loa loa* **and** *O. volvulus* **by Diethylcarbamazine Chloride.**] *Ann. Soc. Belge de Méd. Trop.* 1949, Mar. 31, v. 29, No. 1, 19–22.

The author describes 3 cases of loiasis and 2 of onchocerciasis treated with Hetrazan, *i.e.* diethylcarbamazine [this *Bulletin*, 1948, v. 45, 532; 1949, v. 46, 275, 565].

Case 1.—Male—47 years. Eighty-one kgm. with Calabar swellings for more than 18 months. No microfilariae in blood. He took 0·3–0·4 gm. Hetrazan three times daily for a total of 3 gm. Has remained free from symptoms 8 months.

Case 2.—Male—60 years. Eighty kgm. Calabar swellings for more than 15 months. Microfilariae present in blood. The first two doses of 0·2 gm. Hetrazan caused pyrexia (38·2°C.) and rigors. Total dosage 3 gm. Four months later he had a relapse (Calabar swelling) which was not treated.

The third case was similar.

The other two cases are said to have been "*gale filarienne*" although microfilariae were never demonstrable. When Hetrazan was given the usual allergic reaction was delayed or absent, so the diagnosis remains doubtful. The patients seem to have improved after treatment. When Hetrazan is given to cotton rats infected with *Litomosoides carinii*, it does not kill the adult worms. *F. Hawking*

WANSON, M. L'Hetrazan dans la période d'invasion de l'onchocercose. [**Hetrazan during the period of Invasion of Onchocerciasis.**] *Ann. Soc. Belge de Méd. Trop.* 1949, Mar. 31, v. 29, No. 1, 85–9.

Hetrazan is effective in destroying the microfilariae of *Onchocerca* in the skin but it is less effective against the adult worms, which completely resist the course of 21 days. Three months after such a course, excision of nodules shows living and apparently normal adult males and females. The present paper refers particularly to a patient treated during the incubation period. A European aged 43 years was bitten on September 21st, 1948, by three *Simulium damnosum*, which were afterwards dissected. One contained five infective larvae. Forty-eight hours later the calf of the patient's leg was oedematous, white, and itching for 2½ cm. around an insect bite. The patient had previously been exposed to *Simulium* bites, but he had not previously responded in this fashion. On October 1st, the swelling had spread round the ankle and was different from the usual reaction to *Simulium* bites. By October 15th, the skin resembled "*peau d'orange*" and was finely papular. During all November, the patient suffered from lassitude and insomnia. On December 2nd, examination showed pachydermia of the lower part of the leg and of the dorsum of the foot, with three hyperpigmented plaques. No microfilariae could be found, but there was an eosinophilia of 12 per cent.

On December 3rd to 5th, there was a general urticarial reaction over the trunk and extremities; this was relieved by antihistamine treatment. By December 25th, the local symptoms in the leg were worse and the patient had lost 3 kgm. in weight. Treatment was started with Hetrazan which immediately

caused exacerbation of the pruritus and local symptoms, controlled by Histaphen. The dosage of Hetrazan was 150 mgm. three times daily for 17 days.

On December 31st, there was definite clinical improvement of all symptoms but there was intense lassitude.

On January 9th, the skin had become thin and supple again ; and by February 28th the patient was completely cured.

This history is interpreted as being a developing infection of *Onchocerca* which was cut short by Hetrazan. [An interesting and instructive case ; the original paper should be consulted for the full details.] *F. Hawking*

KERSHAW, W. E. **Observations on** *Litomosoides carinii* **(Travassos, 1919) Chandler, 1931. II. The Migration of the First-Stage Larva.** *Ann. Trop. Med. & Parasit.* 1949, Apr., v. 43, No. 1, 96–115, 6 figs. [29 refs.]

" 1. A series of experiments are described in which a direct, as distinct from an indirect, attempt was made to define the time taken by the first-stage larva of *Litomosoides carinii* to migrate, immediately after birth, from the adult female, through the pleural space, to the peripheral circulation. With uninfected cotton rats as recipient hosts, adult female worms were transplanted to the pleural cavities, pleural exudate containing developing larvae was injected into the pleural cavities, and blood containing fully developed larvae was injected intravenously into the pleural and peritoneal cavities and into the subcutaneous tissues.

" 2. The migration-time from each of these sites, though variable, was found to be commonly one day, though in one experiment larvae were found in the peripheral circulation one hour after the surgical transfer of worms. The variability in the results was too great for differences in the migration-rates of larvae in different stages of development to be defined ; nor was the age of an infection found to affect the results.

" 3. The persistence of the larvae in the peripheral circulation was found to vary from days to weeks or even months.

" 4. These results are compared with observations on other filariae, and the necessity is stressed of observing host-parasite specificity and of using large numbers of larvae in such experiments, in order to allow for uneven distribution in the recipient host.

" 5. The rapid and urgent development of the larva of *L. carinii* to attain a form infective to the next host, and its persistence in the site where an optimum opportunity of transfer is presented, are compared with the corresponding developmental stages of other nematodes parasitic in man, animals and plants, and are found to be not inconsistent with them."

LAGRANGE, E. Essais de chimiotherapie sur la filaire (*Icosiella neglecta*) de la grenouille (*Rana esculenta*). [**Chemotherapeutic Studies on the Filaria** (*Icosiella neglecta*) **of the Frog** (*Rana esculenta*).] *Ann. Parasit. Humaine et Comparée.* 1949, v. 24, Nos. 1/2, 49–53, 1 fig. & 1 pl.

Frogs (*Rana esculenta*) collected at two places in France had an infestation rate of 15–35 per cent. with *Icosiella neglecta*. Other frogs were obtained from Léopoldville and microfilariae (and a few adults) were found in *R. galamensis* and *R. occipitalis*. Antifilarial activity has been found in two of a series of compounds tested :

(1) Methyl violet. This kills the microfilariae of *Dirofilaria repens* at 1 : 400,000 in 17 hours. When given intravenously to frogs, it seems to have some action in killing or sterilizing the adult female worms although the microfilariae are unaffected. Unfortunately this compound proves toxic in the rat and the dog and high doses cause pulmonary oedema.

(2) Dipharsine U.C.B. (hydrochloride of oxyamino-phenyl-dichlorarsine, *i.e.* oxophenarsine). When this was given to a patient infected with *Loa* it caused transient improvement of his symptoms. When injected into frogs it caused death of most of the adult female worms although the microfilariae were more resistant. [Many organic arsenical compounds show marked filaricidal powers against the adult worms of *Litomosoides* in cotton rats.] *F. Hawking*

SCHÜFFNER, W. & SWELLENGREBEL, N. H. **Retrofection in Oxyuriasis. A Newly Discovered Mode of Infection with** *Enterobius vermicularis*. *J. Parasitology*. 1949, Apr., v. 35, No. 2, 138–46, 6 figs.

Hitherto, oral ingestion of the eggs of *Enterobius vermicularis* has been thought to be the only method of acquiring this parasite. During an investigation lasting for five years, the authors discovered that another method exists, wherein the larvae, having hatched from eggs deposited in the peri-anal region, re-enter the body *via* the anus and migrate upward to the caecum, where they grow to maturity. For this unique helminthological phenomenon the new word " retrofection " is coined. Thus, to the existing knowledge concerning the well-lubricated machinery of dissemination and transmission which characterizes the life-cycle of what might justly be termed " man's most personal parasite ", there is now added a further refinement of procedure whose implications have yet to be fully explored. The biological curiosity attaching to the life-cycle of *E. vermicularis*, as exemplified by the external migration and death of the gravid females and the rapid incubation of the eggs, is much enhanced by this finding, which not only reveals an unparalleled phase in the known man-helminth relationships, but opens up a new line of study in the wide range of hosts which harbour oxyurid worms. From the medical aspect, it will explain much that has been perplexing about the refractory nature of pin-worm infections, and it indicates at least one new approach in prophylaxis. Of importance too, is the effect it should have in reducing if not obliterating the stigma of uncleanliness which sometimes is unhappily associated with pin-worm infection in adults.

Before proceeding with the main theme of the paper, the authors demonstrate by means of graphs showing the results of daily anal egg recoveries on infected persons over long periods of time, that in the case of oral ingestion of eggs different pictures of the infection are produced by different modes of egg transmission. Three modes are discussed: 1. Direct transmission by fingers. 2. Indirect transmission, or secondary contamination of food and fingers. 3. Dust-borne transmission.

1. Direct transmission from the anal region to the mouth is common in children, rare in adults and produces a picture of chronic, heavy infection, which is terminated at least temporarily by treatment.

2. This method involves both children and adults. In adults there is spontaneous self-cure in the absence of re-infection, but in children self-cure is prevented by continuation of finger transmission. Less intense infections result from this method.

3. Dust-borne transmission is common in schools where the environment is favourable and results in chronic but light infections which appear intermittently throughout the year. It is largely responsible for the widespread distribution of pin-worms.

Proof of the existence of the hitherto unknown " retrofection " was obtained experimentally and it was observed to have occurred naturally in circumstances which allowed no other possible interpretation. The idea had its inception in

the known fact that larvae have occasionally been found crawling on the anal region, having hatched out "precociously" and presumably to no purpose. In the experimental work, eggs were hatched out in artificial gastric juice and the larvae were applied to the sphincter portion of the anus in two human volunteers. One of these was treated thus with about 100 larvae and the other (the senior author of the paper) with about 150 larvae. Both subjects became infected after pre-patent periods of 76 and 43 days respectively. A third volunteer, aged 22 years, who had been proved negative for oxyuriasis for about 5 months previously, was inoculated peranally with 50 larvae and became positive after an incubation period of 76 days. Two of these subjects subsequently provided natural evidence of retrofection when, after a period of freedom from infection, they again became positive. Re-examination of previous data also confirmed the existence of retrofection.

It is remarked that retrofection probably occurs in children but is difficult to prove as it is likely to be masked by the occurrence of oral transmission. In adults, however, although as shown by the Amsterdam experiment it does not invariably occur, it should be suspected in all cases of chronic oxyuriasis. It would present a picture of recurrent infection at periods not exceeding the life-span of the worms, *i.e.* 37 to 93 days, since one generation must follow another in succession. "It will now be the task of the family physician to investigate to what extent retrofection is common in adults. Once recognized, termination of the infection can be achieved without drug therapy. Since it is known that these infections can end spontaneously, mechanical prophylaxis must be employed to achieve the goal of interrupting the chain of recidives. This is done by removing, for a certain period of days, the eggs from the anal region before the larvae have a chance to hatch, that is, every 6 hours, the time required for the enclosed embryos to mature in air."

J. J. C. Buckley

HÄNEL, L. & WEISS, R. Beitrag zur Wurmtherapie. [**Contribution on the Treatment of Helminthiasis.**] *Deut. med. Woch.* 1949, June 10, v. 74, No. 23, 745–6.

The author refers to previous correspondence on the treatment of enterobiasis and tells of the success he has had with phenothiazine, known also under the names dibenzothiazine and thiodiphenylamine, commercially as Contaverm, the dose being one tablet thrice daily for a child, two for the adult. It is insoluble in water or dilute acid or alkali. When oxidized it becomes more soluble, is absorbed and excreted in the urine which it colours a reddish brown. It does not cause untoward symptoms such as nausea and vomiting as may crystal or gentian violet. Some have reported it as causing anaemia [this *Bulletin*, 1946, v. 43, 940] but that, in the authors' opinion, was due to excessive dosage. They gave 7 gm. in 4 days, whereas the present authors advise doses up to 6 gm. spread over 5 days, for a patient weighing 60 kgm. and dosage according to weight, not age. For children he gives 7 to 15 tablets of "Contaverm", *i.e.* 1·4 to 3 gm. of phenothiazine, spread over 5 days. Details are given of two patients, a boy of 5 who had had the infection for two years, and a woman of 37 years. Both had had intractable pruritus and resultant eczema. These distressing symptoms cleared up in 4–5 days and the worms a day or two later, the dose being one tablet thrice daily for the child, two for the adult. Although the symptoms cleared up the course was repeated after an interval of three weeks, the child being given half the former dose. During observation for several months there had been no signs of any recurrence.

H. Harold Scott

RIEDEL, B. B. & LUNDE, M. N. **The Comparative Effect of some Sulfonamides on Experimental Trichinosis in White Mice.** *J. Parasitology.* 1949, June, v. 35, No. 3, 261–6. [19 refs.]

" The effect of several sulfonamides on trichinae was studied. The sulfonamides were incorporated in rations at nontoxic levels. These rations were fed to two series of mice immediately after infection with 100±5 *T. spiralis* cysts until autopsied. When the numbers of parasites harbored by the sulfonamide fed groups of mice were compared to the numbers of parasites harbored by the control mice, it was found that sulfanilamide fed to mice at a two per cent concentration caused an over-all larval reduction of 54 per cent. The effect of sulfaguanidine on trichinae at a two per cent level was slight and doubtful. Rations containing one per cent sulfapyridine, one per cent sulfathiazole or 0·5 per cent. sulfadiazine were ineffective on the parasite."

STEIN, Kathryn F. **Effect of Cortical Extract and other Agents on Eosinophilia of Mice infected with** *Trichina spiralis.* *Proc. Soc. Exper. Biol. & Med.* 1949, June, v. 71, No. 2, 225–6.

ALICATA, J. E. & BURR, G. O. **Preliminary Observations on the Biological Effects of Radiation on the Life Cycle of** *Trichinella spiralis.* *Science.* 1949, June 10, 595–6, 1 fig.

Irradiation of trichinous meat under certain conditions did not kill the encysted larvae, but rendered sterile a proportion of the female worms which developed when the encysted larvae were given in food to experimental animals.

Specimens of trichinous rat meat, each of 1 gramme, were placed in a refrigerator at 4°C. between two tubes containing radio-active cobalt. The irradiation dose received by the meat was estimated to be 2,000 r for each 24 hours and consisted largely of gamma rays, the beta rays having been filtered out. The irradiated meat was then given to white rats which were subsequently killed and examined for intestinal and muscle infection. It was found that irradiation for 4 days affected 12 to 86 per cent. of the resulting females, in that the ova in the uterus failed to become embryonated. The remainder showed embryos in the uterus. Irradiation for 5 days sterilized 45 to 100 per cent. and for 6 days, 60 to 100 per cent. of the females. Female worms which were not sterilized produced larvae which invaded the muscles in the normal way. In addition to becoming sterile, some of the female worms showed abnormal morphological changes, in the form of vesiculation and irregular elevations of the body-wall. Further experiments are in progress to test the effect of larger doses of irradiation for a shorter time from a more intense source. *J. J. C. Buckley*

DEFICIENCY DISEASES

BARAKAT, M. R. & SMITH, Dean A. **Plasma-Protein Levels in West Africans.** *Lancet.* 1949, July 2, 12–13.

Such limited reports on plasma-protein levels in Africans as are available indicate that these are towards or above the upper limit of what is taken to be the normal range for Europeans, *i.e.* 6·0–8·5 gm. per 100 ml. [this *Bulletin*, 1937, v. 34, 548 ; 1946, v. 43, 866 ; 1948, v. 45, 810].

The present authors, in the course of a nutrition survey (to be reported fully later) in the Gambia, studied the plasma-protein levels of 447 people in two villages in the Middle River Division. Clinical and dietary evidence was found of deficiency of calories, vitamin B complex and possibly some protein components.

In Genieri village, plasma-protein values of 319 persons (155 males, 164 females) were determined: their ages ranged from 0 to 16 years and over. The mean levels found varied from 6·42 to 7·70 gm./100 ml. with a tendency to rise with age. Haemoglobin levels (Sahli) averaged from 47·6 to 78·2 per cent. within the five age-groups, also with a tendency to rise with age.

The corresponding figures for Jamar village, where 128 persons (66 males, 62 females of 6 to 16 years and over) were examined, were 7·93 to 8·14 gm. protein per 100 ml. and 72·4 to 78·8 per cent. haemoglobin.

The detailed figures are shown in a table.

Eighteen adults had oedema, apparently nutritional, but not due to vitamin B_7 deficiency. Their mean plasma-protein level was 7·66 gm./100 ml. (5·93 to 8·80).

The investigation is progressing with special reference to diet and the presence of protozoal parasites. *H. J. O'D. Burke-Gaffney*

SMITSKAMP, H. Voeding en aanpassing aan het tropenklimat. [**Nutrition and Adaptation to a Tropical Climate.**] *Med. Maandblad.* Batavia. 1949, May, v. 2, No. 5, 129–33.

In any tropical climate there is a tendency to ascribe vague symptoms such as anorexia, lassitude, irritability and constipation to defective acclimatization. This diagnosis is often correct but in some cases the syndrome is due to nutritional deficiencies.

Two cases are described in which the above symptoms were associated with a dislike of the rice dishes, of which the East Indian diet is largely composed. Both patients were taking diets grossly defective in both protein and vitamins, especially vitamin B_1. One had some objective signs of hypovitaminosis, the other had none. Both were encouraged to take a fuller diet and were given vitamin supplements. After an interval both recovered completely.

The importance of remembering the possibility of nutritional deficiencies when dealing with such cases is stressed. *A. L. Winner*

PANTRIDGE, J. F. **Cardiac Lesions in Thiamin Deficiency.** *Brit. Heart J.* 1948, Oct., v. 10, No. 4, 252–62, 16 figs. [25 refs.]

Heart-block and other manifestations of impairment of conduction have sometimes been recorded in cases of human beriberi; the present experiment in which pigs, known to be particularly susceptible to vitamin B_1 deficiency, were used as experimental animals, was undertaken to study the effect on cardiac conduction of prolonged, severe deficiency of this factor.

After 40–60 days on a thiamin-free diet all four experimental animals developed bradycardia, sinus arrhythmia and electrocardiographic changes. Later all developed some degree of heart-block, which was complete in two cases. The control animals showed no changes throughout. The pigs with heart-block were each treated once with 2·5 mgm. of thiamin, which restored A-V conduction to normal within 48 hours. Thereafter the deficient diet was continued; three pigs died of beriberi on the 64th, 74th and 116th days, the fourth was sacrificed on the 157th day.

At postmortem no evidence of subcutaneous oedema was found. Myocardial lesions were most marked in the auricles and auricular septa. The ventricular

lesions were confined almost entirely to the Purkinje cells, which showed acute hyaline necrosis.

These findings accord with clinical experience in human cardiac beriberi; initial biochemical changes causing disturbance of the conducting mechanism are reversible, but may develop into irreversible morphological lesions.

Dean A. Smith

AUFFRET, C. & TANGUY, F. Considérations sur 139 dosages de vitamine C dans le sang de militaires africains de différentes unités de Dakar. [**Notes on 139 Estimations of Blood-Vitamin C Levels in African Soldiers.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 77–80.

Of 99 soldiers of different races and varied length of service at Dakar, 77 had blood ascorbic acid levels of less than 4 mgm. per litre. All but three of a group of 40 recruits from Dahomey showed similarly low levels and in none did the level exceed 7 mgm. per litre. These levels indicate definite depletion. Bleeding gums were found in some subjects of the latter group, but frank scurvy was rare.

The authors discuss the relationships of vitamins C and P to each other and to the causation of the haemorrhagic manifestations associated with scurvy and pre-scorbutic states. [They quote numerous authorities but give no references.]

Dean A. Smith

AUFFRET, C. & TANGUY, F. Vitamine C dans les organes d'enfants et d'adultes africains de la région dakaroise. [**The Vitamin C Content of the Organs of African Children and Adults in the Dakar Area of French West Africa.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1948, v. 5, No. 1, 167–72.

Estimations of vitamin C were carried out on the liver, spleen, pancreas, kidneys, heart and suprarenals of 27 persons who had died of apparently non-nutritional causes. The results were compared with those found in three tuberculous subjects whose ascorbic acid excretion, measured shortly before death, had indicated saturation.

The average levels in the nutritionally " normal " subjects were much lower, of the order of half, than those in the saturated subjects.

Although none of the persons showed any clinical evidence of deficiency the authors consider that their functional efficiency and capacity for work must have been greatly impaired. A plea is made for extended dietary use of the many good fruit and vegetable sources of vitamin C available locally, especially the fruit *Detarium senegalense.*

Dean A. Smith

See also p. 913, RAOULT, AUFFRET, TANGUY & MARTIN, **L'acide ascorbique dans le traitement de la fièvre bilieuse hémoglobinurique.**

SPRUE

SAINT-ETIENNE, J. La sprue tropicale. Considérations pathogéniques. [**Observations on the Pathogenic Features of Tropical Sprue.**] *Méd. Trop.* Marseilles. 1948, Nov.–Dec., v. 8, No. 5, 571–86. [Numerous refs.]

This article is a résumé of the various investigations conducted mainly by Anglo-American workers during the recent war. This renders it almost impossible to write a summary of the numerous investigations which have been adequately reviewed in this *Bulletin.*

There are several misprints especially with reference to the spelling of English surnames.

P. Manson-Bahr

WOODRUFF, A. W. **Aetiological and Prognostic Features in Tropical Sprue. A Study of 47 Cases over a 2¾–3 Year Period.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, May, v. 42, No. 6, 605–12, 1 fig. [12 refs.]

The subjects of the paper are 47 patients with tropical sprue admitted to an R.A.F. mobile field hospital serving members of the Air Force in the Chittagong area, from July 1944 to June 1945. "There was a tendency for the cases to occur in small groups among personnel of individual units."

A figure shows that the rise and fall of the monthly incidence curve of the 47 cases of sprue (month of onset of symptoms) almost coincides with, but actually slightly precedes, the incidence curve of 72 cases of amoebic dysentery. The peaks fall in July and the trough of the sprue curve from November to March.

The duration of service in India before onset was 6 to 12 months in 27 per cent., 12 to 18 months in 16·2 per cent., 18 to 24 months in 16·2 per cent., 24 to 30 months in 19 per cent., 30 to 36 months in 16·2 per cent., and 3 years and over in 5·4 per cent.

The most frequent symptoms were :—diarrhoea in all cases, with an average duration of 3·73 months ; tongue lesions in 39, including 19 with active ulceration ; loss of weight in all cases, average loss 28 lb. ; abdominal distension and flatulence in all, severe in 20 cases. Less constant symptoms were loss of appetite, nausea and vomiting, and cramps in the legs. Anaemia was not a striking feature ; the average red cell count was 3·94 million, and the colour index 1·06. Faecal fat was estimated in 22 cases ; the total fat was 37·12 per cent. of dried faeces and the split fat 28·64 per cent. ; split fat was therefore 77·15 per cent. of total fat.

At the end of 2¾ to 3 years the author was able to trace 34 patients. All were in full work. Twenty-nine had gained weight and the average gain in weight of the 34 patients was 24 lb. All patients stated that they were free of diarrhoea, but 23 had had some diarrhoea, usually of a very transitory nature, at some time since their return to Britain, 6 men had had 4 or more attacks of short duration and 3 others one attack lasting 1 to 2 weeks. Eleven complained of ulcers on the tongue at some time. Occasional attacks of abdominal discomfort and distension were complained of by 6 men and frequent attacks by 3 others. Only 3 men "considered that their energy was still significantly impaired". *L. E. Napier*

FOX, H. J. **A Comparison of Pteroylglutamic Acid and Liver Extract Maintenance Therapy in Sprue.** *New England J. of Med.* 1949, May 19, v. 240, No. 20, 801–3.

There have been conflicting reports on the haematological response of sprue to treatment with synthetic folic acid. Seven patients with sprue, all previously treated for years dietetically and with liver and vitamin preparations, were given synthetic folic acid for at least a year. In general the effect was beneficial, in the majority of the patients there was a lessening of diarrhoea and a gain in weight : one patient, in spite of a daily oral dosage of 60 mgm. of folic acid, suffered from increasing steatorrhoea, glossitis, loss of weight and other manifestations of severe sprue ; she proved as unresponsive to purified liver preparations as to folic acid, but responded to massive intravenous doses of a crude liver preparation. The requisite dosage of folic acid in the cases which benefited from it was found to be from 15 to 30 mgm. daily ; a 5 mgm. daily dose, advocated by others, proved seriously inadequate. In spite of the distinct clinical improvement in some cases the figures for haemoglobin, the red cell count, and haematocrit readings were found after a year of folic acid treatment to be lower than after liver treatment. *A. R. D. Adams*

HAEMATOLOGY

Correction

In his abstract of a paper from the *Lancet* by LEHMANN on Macrocytic Anaemia in Central Africans [this *Bulletin*, 1949, v. 46, 664] the abstracter queries the use of the word "coctic." The word should in fact have been "precoctic." Since the paper was written, a note has appeared in the *Lancet*, 1949, January 22nd, 169, in which it is explained that the word "coctic" was printed in the original article through a series of errors, and the editorial explanation goes on to state:—

"Dr. Lehmann's paragraph introducing the word should have read as follows:—

"The reticulocytes and cells in the early postreticulocytic stage are here called precoctic cells. By precoctic blood picture is meant one due to a condition where large cells are produced in regeneration, the macrocytosis not being due to a disturbance of bone-marrow function by the absence of essential nutrients but being, on the contrary, caused by a hyperactivity of the marrow which leads to an emission of slightly 'unfinished' cells (coctus=fully mellowed). To call these cells immature might suggest an inhibition of cell production at the nucleated stage, and the term 'regenerative' would not differentiate from a state where regeneration proceeds without macrocytosis."

PATEL, J. C. & BHENDE, Y. M. **Synthetic Folic Acid in Tropical Macrocytic Anaemia.** *Indian J. Med. Sci.* 1949, June, v. 3, No. 6, 367–75.

An account of six cases.

SINN, H. J. **Cooley's Anaemia: Report of a Case.** *Med. J. Australia.* 1949, Apr. 30, v. 1, No. 18, 579–81, 1 fig.

Stated to be the first recorded case in Australia.

SCHWARTZ, S. O. & MASON, J. **Mediterranean Anemia in the Negro. A Report of Four Cases and their Families.** *Blood.* 1949, June, v. 4, No. 6, 706–21, 4 figs. [26 refs.]

"Four cases of 'Mediterranean anemia' are reported in Negroes.

"The hematologic and clinical findings of available relatives are presented.

"The disease in the Negro resembles the condition as found in people of Mediterranean ancestry in every particular."

VAN DER SAR, A. De sikkelcelziekte. [**Sickle-cell Anaemia.**] *Nederl. Tijdschr. v. Geneesk.* 1949, June 4, v. 93 (ii), No. 23, 1867–74, 5 figs. on pl. [Refs. in footnotes.] English summary.

A full review of the literature of sickle-cell anaemia is given and the symptomatology reviewed. Three negro sisters are then described, all of whom had sickle-cells in the blood and had recurrent crises with fever, icterus and anaemia. All have so far recovered from their crises. The family history is given: both parents had sickle-cells in the blood without symptoms. Of the ten children, all five sons were free from the disease, two daughters had latent "sicklaemia" and three daughters had recurrent sickle-cell crises.

These cases occurred in Curaçao. Blood examinations were carried out on 2,499 inhabitants, of whom 10·7 per cent. had sickle cells in the blood, 9·4 per cent. males and 12·3 per cent. females.

Striking changes in the bones are seen in these cases, mainly thinning of the cortical bone, osteoporosis and variations in density. The skull often shows a phenomenon termed " hair on end sign " or " *signe en brosse*", the outer table disappearing and the diploë appearing striated.

The spleen also shows marked changes, including calcification. Treatment is symptomatic. Splenectomy has proved disappointing. *A. L. Winner*

VENOMS AND ANTIVENENES

CECCALDI, J., TRINQUIER, E., ARNOULT, H. & PELLISSIER, A. Sur quatre cas d'envenimation par morsures de " vipéridés " observés à l'Institut Pasteur de Brazzaville (Afrique Équatoriale Française). [**Four Cases of Snakebite at the Brazzaville Pasteur Institute.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 1/2, 38–43.

These four cases occurred among the employees at the Pasteur Institute, Brazzaville, French Equatorial Africa. One was bitten by a *Bitis arietans*, one by *B. nasicornis*, and two by *B. gabonica*. The symptoms were very similar in kind, though varying in degree. Three were bitten on the right thumb (one of them twice) and the other on the left hand. The symptoms were severe pain, rapid and extending swelling and, later, haemorrhage. All recovered in a few days, but in the case of the first there was some residual weakness of the muscles and stiffness of the forefinger, though 6 years had elapsed. One of the *B. gabonica* was only 3 weeks old, but the effects of its bite were very serious and a second injection of antiserum was called for. The dose given was 20 cc. In the case of the attendant bitten by *B. arietans*, the antiserum was obtained from the South African Institute for Medical Research ; one of those bitten by a *B. gabonica* received the locally prepared antivenin ; for the other two the source of antivenin is not mentioned but would appear to have been the Johannesburg Institute serum. The locally prepared serum is polyvalent for the Viperidae *B. gabonica* and *B. nasicornis*, and the Colubridae *Naja nigricollis* and *N. melanoleuca*. Other local snakes are *B. arietans*. *Causus rhombeatus*, *A. squamiger*, *Dendraspis* and *Boulangerina annulata*, but these are rarely caught so that their antivenins are prepared locally only occasionally.

H. Harold Scott

ABALOS, J. W. Cuales son los animales venenosos de la Argentina ? [**What Poisonous Fauna are there in the Argentine ?**] *Universidad Nacional de Tucuman : Instituto de Medicina Regional. Publicación No. 481.* 1949, 24 pp., 16 figs.

This article names the commonest of the venomous animals—including in this term fish, snakes, spiders and scorpions—to be found in the Argentine. The author adds a few remarks on some of these, but of an elementary character.

In the section on snakes the author indicates by diagrams the different dentition of the aglypha, opisthoglypha and proteroglypha and then proceeds to name the chief species, namely, *Crotalus terrificus*, 7 species of *Bothrops* (locally known as *yarará*) of which the chief are *B. atrox*, *B. cotiara*, *B. jararaca* and *B. jararacussu*, the others being *B. alternatus*, *B. neuwiedii meridionalis* and *B. ammodytoides* ; three species of coral snake, *Micrurus lemniscatus*, *M. corallinus* and *M. frontalis*, the first of these found all over the Argentine. There are also several species of " false coral snake", very like the true venomous ones, but the peculiar colour markings are only on the dorsum whereas in the

true Coral snakes the markings go quite round the body. A line map shows clearly the distribution of the snakes mentioned. There is also the "black snake", *Pseudoboa cloelia*, a mortal enemy of the poisonous snakes which it fights relentlessly and eats when it has subdued them. It is coloured a slatey black dorsally, dull white ventrally with some red scales on the sides; it is about 2½ metres in length, is slender and agile; it does not attack man and does not resent being handled.

Of spiders the most venomous is *Latrodectus*, especially *L. mactans* (the Black Widow) and *L. geometricus*. There are, says the author, 40 species of scorpion in the Argentine, but the only one mentioned by name is *Tityus vittatus* which gives a painful sting but without sequelae. The venom of some "appears to have an analgesic effect." The whole subject of scorpions and their venoms in the Argentine needs to be studied. *H. Harold Scott*

DERMATOLOGY AND FUNGUS DISEASES

MONTEL, M. L. R. Dermatites verruqueuses hyperkératosiques. [**Hyperkeratotic Verrucous Dermatitis.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 5/6, 190–93, 4 figs. on 2 pls.

The following is a translation of the author's summary.

Three cases of verrucous dermatitis seen in Cochin China are recorded. The attention of clinicians is drawn to the hyperkeratoses of the lower limbs so frequent in the tropics and of which the nature, aetiology and pathology are very obscure.

[The paper is illustrated with four photographs of lesions of the foot.]

H. J. O'D. Burke-Gaffney

DI PIETRO, A., NIÑO, F. L. & COSTA, L. P. Histoplasmosis o reticulohistiocitosis parasitaria con localización lingual. [**Histoplasmosis of the Tongue.**] *Rev. Asoc. Med. Argentina.* 1949, May 15–30, v. 63, Nos. 653/654, 229–31, 6 figs. [27 refs.]

The English summary appended to the paper is as follows:—

"In a man, 52 years old, the authors report the clinical and histopathological study of localized Darling's histoplasmosis or parasitary reticulo-histiocytosis of the tongue by *Histoplasma capsulatum*.

"This case would be the 4th of histoplasmosis in Argentina."

BASS, H. E., SCHOMER, A. & BERKE, R. **Question of Contagion in Coccidioidomycosis. Study of Contacts.** *Amer. Rev. Tuberculosis.* 1949, June, v. 59, No. 6, 632–5.

It is probably true of all the systemic mycoses, caused by "dimorphic" fungi, that infection is not transmitted directly from man to man except in rare accidental cases associated with *post mortem* examinations or surgical operations. However, ROSENTHAL & ROUTIEN [this *Bulletin*, 1948, v. 45, 467], by instilling directly into the bronchial tree of guineapigs the infected sputum and pus from human cases of coccidioidomycosis, succeeded in infecting the animals, and this, they contended was evidence of the probable direct transmissibility of the disease. The present paper, which is a timely refutation of the view of Rosenthal and Routien so far as natural infection in man is concerned, records the careful observations made on 11 intimate contacts

(wives, sons, daughters, brothers, sisters, etc.) of 7 ex-soldiers suffering from persistent coccidioidal infection; six with pulmonary cavitation and the seventh with disseminated disease involving both skin and lungs. The periods of exposure of the contacts ranged from 6 months to 5 years, and all the persons concerned were resident in New York City, far removed from the endemic centres of the disease. The observations on the contacts, which included repeated coccidioidin skin tests and X-ray examinations of the chest, yielded no evidence whatsoever of infection. *J. T. Duncan*

TROPICAL ULCER

Rao, V. R., Kini, M. G. & Subrahmanyan, K. S. **Tropical Ulcers in Madras City.** *Indian Med. Gaz.* 1949, Mar., v. 84, No. 3, 88–92, 15 figs. on 3 pls. [10 refs.]

This article is based on 38 cases of tropical ulcer treated at the Stanley Hospital, Madras, from December 1946 to the end of February 1948. No age was immune but most of the patients were below 30, and 32 were males and 6 females. Those employed in hard labour and living in insanitary conditions were more prone to this condition than others (19 out of 38 cases). Most of the patients had a history of a fortnight to a month's duration and the general experience was that the maximal incidence occurred during and after the monsoon months (in 1947 the monsoon failed in Madras). Fifteen patients had multiple ulcers and there were 60 ulcers in 38 cases, one patient having as many as eight. Except in rare instances the ulcers were found below the knee, and were "of the size of a pea to that of the old silver rupee or even bigger in a few cases." They were very painful and acutely tender, and the general condition of almost all the patients was poor.

Fusiform bacilli and *Treponema vincenti* were found in most cases, but one showed only spirochaetes and a mixed infection of staphylococci, streptococci and *Ps. pyocyanea* without fusiform bacilli [was this a case of true tropical ulcer ?]. The culture medium used consisted of nutrient broth 100 cc., agar 1·5 gm., sterile defibrinated human blood, 25 cc. Difficulty was found in obtaining pure cultures by surface inoculation. In 13 cultures fusiform bacilli were grown in 6 cases.

On admission every patient was given a wash with sterile normal saline and thereafter a saline dressing was applied for 24 hours; during treatment repeated study of the organisms was made. Out of 60 ulcers, 48 were treated with penicillin in a strength of 1,000 units in one cc. of pyrogen-free distilled water; this was with a Holmspray and the ulcer covered with a sterile dressing. With full compression of the rubber bulb the amount of penicillin sprayed amounts to 270 units. The dressing was changed once daily and all cases were treated as out-patients. Penicillin was discontinued as soon as the ulcer began to heal and the discharge became scanty; thereafter a thiazamide paste or a 1 per cent. aqueous solution of gentian violet was used. Large ulcers took an average of 28 days to heal and the average amount of penicillin required for a case was 1,300 units (maximum 7,000). With 2 or 3 dressings even the worst cases were relieved of pain and the discharge was lessened. Eight ulcers were dressed with Marfanil powder (para amino methyl benzene sulphonamide hydrochloride). When *Ps. pyocyanea* or *Proteus* was present response to penicillin was poor, but Marfanil was found to be effective. The cost of

Marfanil is high and penicillin is regarded as the drug of choice in the ordinary case. [No reference is made to any attempt to treat the general condition of the patient.]

C. F. Shelton

KNOLL, H. Zur chirurgischen Behandlung des tropischen Ulcus. [**The Surgical Treatment of Tropical Ulcer.**] *Acta Tropica.* Basle. 1949, v. 6, No. 2, 145–9, 5 figs.

MISCELLANEOUS DISEASES

SPITZER, H. **Essential Hypertension on the Island of Curacao.** *Ann. Western Med. & Surgery.* 1949, Apr., v. 3, No. 4, 133–5.

The incidence of hypertension is very high both in the coloured and indigenous white population in the island of Curaçao, and this investigation was done to determine the relationship between constant dehydration and hypertension, the study being based primarily on an examination of school children. Most of the children were coloured, they were of both sexes, between the ages of 6 and 18, and of average health. More than 1,000 diastolic and systolic readings were made by the auscultatory method, and 898 school children were examined ; the remainder were adults, most of whom had hypertension.

School children : The readings were based on the systolic level as it was found that the diastolic rise followed the systolic after some delay. The degree of hypertension was striking ; thus 7 children between the ages of 10 and 16 had a blood pressure of over 160 mm., while 2 aged 6 years had one of 130–139 (systolic). In all the age groups the average was well above the normal. Over 100 blood volume estimations were done by the Congo Red method, which gave consistent results on repeated application to the same patient, and there was correlation between deficit in blood volume and increase in blood pressure.

Precipitation per year in Curaçao averages 20 inches, and there is continuous sweating, although not comparable to the amount seen in desert areas. Hypertension in Curaçao does not appear to be related to race, *i.e.*, white people born on the island or who had immigrated in infancy also showed a high incidence of this condition.

[The author's conclusions may appear debatable, and the observations should be repeated in other parts of the world with a similar climate.]

C. F. Shelton

DIEZ DE URDANIVIA, A. & ESTRADA BERG, J. Escleroma. [**Scleroma.**] *Medicina.* Mexico. 1949, May 25, v. 29, No. 580, 192–9, 12 figs.

The authors prefer the term scleroma to rhinoscleroma because the disease attacks other parts than the nose. In one record of 335 cases the vocal cords were attacked in 19·4 per cent., the upper part of the larynx in 12·9, the fauces in 24 per cent. The accompanying Fritch's bacillus, or *Klebsiella rhinoscleromatis*, has not been proved to be the actual cause, because experimental inoculation has so far been negative.

Pathologically, the authors recognize three stages : 1. Atrophic phase, in which the secretion contains the organism ; 2. Nodular, in which the tissue shows Mikulicz cells and Russell bodies and there is infiltration of the nasal cartilage and, perhaps, pharynx and larynx ; 3. Cicatricial. Scleroma and carcinoma may coexist. The treatment suggested comprises autovaccines,

with results at best very dubious, X-rays and radium, and streptomycin, 0·5 gm. morning and evening, to a total of 30–40 gm. After a week of this, symptoms of deafness, tinnitus and vertigo are likely to arise. Four cases are mentioned, but with little detail; in two, operative treatment—extirpation—was carried out; in the other two nothing is said about treatment. There are good photographs of this horrible condition [see this *Bulletin*, 1949, v. 46, 872]. *H. Harold Scott*

PRIEST, W. M. **Acute Meningo-Encephalitis of Uncertain Origin in West African Troops.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, May, v. 42, No. 6, 581–96, 4 figs. (3 on 2 pls.). [29 refs.]

There is a large and growing literature on the neurotropic viruses but little is known about their clinical manifestations in the tropics and few reports have appeared on this subject. The 10 cases here reviewed, mainly from the clinical standpoint, and coming chiefly from Nigeria, were in-patients aged between 19 and 36. Nine occurred during December to March, the driest and hottest time of the year. The cause was believed to be a filterable virus, although as experimental animals were unavailable, definite incrimination of a specific virus was not possible.

The cases described are all examples of an acute illness with sudden onset, fever, headache and, in some instances, meningismus, cranial palsies, hemiplegia and monoplegia. A variable pleocytosis was present in the cerebrospinal fluid together with a marked rise in protein content. Xanthochromia was present in 5 instances (3 fatal). Six of the cases were fatal, and the author considers that the facts suggest infection with a neurotropic virus.

Trypanosomes were not found in the cerebrospinal fluid and no glandular enlargement was present. Of the first 8 patients the 2 who survived received no trypanocidal treatment, and in those who died there were no signs of trypanosomiasis.

A positive blood Kahn is so frequent in West African patients that its presence carries very little weight. Cerebral malaria is rare in West African troops, and moreover all these patients were given parenteral quinine or mepacrine without therapeutic effect.

No evidence of tuberculosis was found in the meninges or elsewhere in any of the fatal cases. None of the patients had been recently vaccinated.

The incidence of neurotropic viruses in the tropics is now increasingly well known. HAMMON and REEVES [*Bulletin of Hygiene*, 1946, v. 21, 14] state that evidence is accumulating that there are a large number of such viruses of man and other animals (arthropod-borne) of "world-wide distribution and no small importance". Search for immune bodies to West Nile virus has shown their presence in the sera of Africans over a wide area of Central Africa. Others such as that called "Semliki Forest virus" [SMITHBURN and HADDOW, this *Bulletin*, 1945, v. 42, 320; 1946, v. 43, 859] have been identified, but little is known of the diseases caused by them in man. *C. F. Shelton*

ALAIN, M., SAINT-ETIENNE, J. & REYNES, V. La mélioidose. Considérations étiologiques, cliniques et pathogéniques à propos de 28 cas. [**Aetiology, Clinical Features and Pathology of 28 Cases of Melioidosis.**] *Méd. Trop.* Marseilles. 1949, Mar.–Apr., v. 9, No. 2, 119–42, 10 charts. [Bibliography.]

The authors report 28 cases of melioidosis from Cochin China and give full clinical details of 10 cases which illustrate the protean manifestations of the

acute, subacute and chronic forms. Nineteen patients are known to have died but a number could not be traced; three have survived for four years after clinical cure. Treatment appears to have been largely surgical.

In no case was the source of infection ascertained and the authors are sceptical of the rodent origin of the disease. Over 20,000 rodents have been examined in Cochin China and many thousands of cultures made from them; only one strain of *Pf. whitmori* has been isolated. Unlike plague, the disease is more prevalent in Europeans than in the indigenous population who are in closer contact with rats. The organism has once been isolated, along with *Ps. pyocyanea*, from the blood of a shaved guineapig immersed in contaminated water. The authors discuss the possible origin of *Pf. whitmori*, considering particularly whether it might be a sudden mutant or an organism usually saprophytic and attaining virulence in debilitated persons. All of their infections arose in subjects debilitated by surgical operations or febrile illnesses, and in some the disease actually appeared after the patients had been a considerable time in hospital. The view is taken that *Pf. whitmori* may be a virulent variant of *Ps. pyocyanea* to which it bears some morphological, cultural and biological resemblance (a view which has previously been expressed by a number of French workers). One worker has demonstrated that certain strains of Whitmore's bacillus produce a soluble green fluorescent pigment in synthetic medium.

This paper contains the most complete list of references on melioidosis known to the abstracter. *J. C. Cruickshank*

PROTOZOOLOGY: GENERAL

BIOCCA, E. Osservazioni sulla posizione sistematica del toxoplasma. [**The Place of** *Toxoplasma* **in Nature.**] *Riv. di Parassit.* Rome. 1949, June, v. 10, No. 2, 73–92. [256 refs.] English summary (9 lines).

More than 40 years ago Nicolle and Manceaux described a protozoon in a rodent in North Africa and named it *Toxoplasma gondii*. Others remarked on its likeness to *Leishmania*, others again to *Encephalitozoon*. Cases of human infection have been reported by Castellani in Ceylon, but Wenyon has cast doubt on these. In short, there seems to have been a certain degree of confusion between *Toxoplasma*, *Encephalitozoon*, *Soroplasma* and *Sarcosporidia*, and the place of *Toxoplasma* in nature is yet to be determined.

From a consideration of this vexed subject the author concludes: 1, that *Toxoplasma*, if it is to be regarded as a protozoon, has a simple morphology (as described in the textbooks), is non-motile, but endowed with a gentle sliding motion (*scivolamento*), capable of infecting many vertebrata, penetrating and multiplying in the tissues; 2, it differs from Rhizopoda, Flagellata, Ciliata and Sporozoa; 3, the reputed species *T. cuniculi*, *T. caviae*, *T. canis*, *T. muris*, *T. hominis*, etc., merely indicate that *Toxoplasma gondii* has been found in different hosts and that there is only one valid species; 3, the genera *Encephalitozoon* and *Soroplasma* have no characters sufficiently valid to separate them from *Toxoplasma*, and therefore, 4, one cannot accept the species of *Encephalitozoon*, *e.g. E. cuniculi*, *E. brumpti*, *E. rabiei*, etc., as valid; 5, *Toxoplasma* and *Sarcosporidia* are easily differentiable, morphologically and biologically, though they have certain characteristics in common. *H. Harold Scott*

MACDONALD, A. **Serological Diagnosis of Human Toxoplasmosis.** *Lancet.* 1949, June 4, 950–53, 1 fig.

Serological tests hitherto used in the diagnosis of toxoplasmosis are technically complicated as in the case of the serum neutralization skin test on rabbits, while the various types of antigen used for complement fixation tests have not been entirely satisfactory; the method used by WARREN and RUSS is one of the best [this *Bulletin*, 1948, v. 45, 1035].

In the account under review, two methods of serological diagnosis were investigated.

In the first, a neutralization test with serum, the strain of toxoplasma was grown on the chorio-allantoic membrane of chicks by a standard technique, the eggs being incubated, after inoculation, for 4 or 5 days at 37°C. The inoculum was the centrifuged deposit from the peritoneal exudate of mice infected by the peritoneal route. Lesions were regularly formed on the chorio-allantoic membrane and the number of these was proportionately reduced by dilution of the inoculum. These lesions, four or five days after inoculation of the egg, are 1–2 mm. in diameter, both ectoderm and mesoderm being parasitized.

The technique of the neutralization tests with serum was essentially the same as that used in virus-neutralization tests.

The sera were inactivated at 57°C. for 20 minutes. Toxoplasma suspensions were prepared from chorio-allantoic membranes with lesions 4 to 5 days old. The membranes were ground without abrasive and suspended in a mixture of 1 volume of broth to 9 volumes of saline (the actual quantities are not stated). The suspension was shaken, allowed to settle for 30 minutes and the supernatant fluid removed. The number of parasites in the fluid was estimated by examination of a stained smear made from a known volume.

In performing the test, the inoculum consisted of a mixture of 0·2 ml. of the inactivated serum and 0·2 ml. of the toxoplasma suspension. This was allowed to stand at room temperature for 30 minutes and was then distributed on the chorioallantoic membrane in 6 eggs which were incubated at 37°C. for 4 or 5 days. Control positive and negative sera were similarly treated. Counts were made of the focal lesions produced.

In reading the tests it was found that the positive sera gave not less than a six-fold reduction in the number of lesions when compared with the control normal serum, showing the presence of neutralizing antibodies.

In complement fixation tests, the antigen used was prepared from infected chorio-allantoic membranes by the method of WARREN and RUSS [details are given in the paper] and a control antigen was similarly prepared from uninfected chorio-allantoic membranes. Preliminary titrations were carried out with known positive and negative sera to determine the optimal dilution of antigen which would give specific fixation with low-titre human sera. In the tests a dilution of 1/18 was found to give maximal titres and was not anticomplementary. The complement fixation test followed orthodox lines. The results were found to be parallel with those obtained by the serum-neutralization test on eggs.

Out of a hundred "normal" sera tested, three fixed complement in a dilution of 120 or more. Two of these three sera were found also to be positive by the serum neutralization test in eggs. The third fixed complement in a dilution of 120 but gave a negative serum-neutralization test in eggs.

The relative values of the different methods of diagnosis of human toxoplasmosis are discussed. *H. E. Shortt*

ENTOMOLOGY AND INSECTICIDES: GENERAL

See also p. 978. COMMONWEALTH INSTITUTE OF ENTOMOLOGY, **Report of the Fifth Commonwealth Entomological Conference.**

PACAUD, A. Observations sur la répartition des gites larvaires de moustiques sur le territoire d'une ville de la banlieue parisienne: Saint-Maur-des-Fossés (Seine) en 1946. [**Observations on the Distribution of Mosquito Breeding Places in the Town of St. Maur-des-Fossés (Seine) on the Outskirts of Paris in 1946.**] *Rec. Travaux Inst. Nat. Hyg.* Paris. 1949, Tome 3. v. 3, 871–8, 1 fig.

——. Expériences relatives à la possibilité d'un côntrole du pullulement des larves de moustique (*Culex*) dans les égouts d'une ville de banlieue (ville de Saint-Maur-des-Fossés, Seine). [**Experiments in the Control of Mosquito Larvae (*Culex*) breeding in the Street Sewers of a Suburban Town (St.-Maur-des-Fossés, Seine).**] *Ibid.* 879–91, 5 figs.

These papers are concerned with the control of house-haunting *Culex* in St. Maur-des-Fossés on the outskirts of Paris. Little or no breeding was observed in pools, ponds, marshes, cesspits, lakes, waterways, nor in boats anchored in the river. But extensive breeding occurred in the precipitation chambers at different points of the street sewer system. This type of chamber is common in Paris and in provincial towns. In summer, larvae and pupae occur in large numbers in these chambers; adults are found on their walls and also in houses. In winter, only a few aquatic stages remain in the chambers and the adult females are found hibernating in large numbers in cellars, caves and stables.

The author discusses the difficulty of treating these breeding places with insecticide. The chambers are subject to recurring vigorous water flow; they often contain a great amount of débris of all sorts from the streets and spider webs are commonly plentiful. Periodic dusting and spraying was consequently found to be unsatisfactory. Complete control was obtained, however, by depositing a small block of plaster impregnated with 50 cc. of a 5 per cent. DDT solution in kerosene in each precipitation chamber. Four treatments in this way between May and September are proposed as probably adequate to control the mosquito during its active breeding season.

Culex pipiens larvae were found during a survey of ponds and ornamental lakes in the town, but no specific identification is given of the *Culex* breeding in the precipitation chambers. *D. S. Bertram*

KING, W. V. & HOOGSTRAAL, H. **Species of *Aëdes* (*Finlaya*) of the *papuensis* Group in the Australasian Region (Diptera, Culicidae).** *Proc. Entom. Soc. of Washington.* 1946, v. 48, No. 6, 135–57, 5 figs.

CARTER, H. F. & ANTONIPULLE, P. **Observations on Sandflies (*Phlebotomus*) in Delft Island, North Ceylon.** *Ann. Trop. Med. & Parasit.* 1949, Apr., v. 43, No. 1, 62–73, 2 figs. & 1 map.

Two visits were made to Delft Island, Ceylon, one from July 22nd to August 19th, 1947, during the dry season and the second from January 9th to 25th, 1948, at the end of the wet season.

Collections of adults of *Phlebotomus* were made both indoors and outdoors in different parts of the island and by means of hand catches, baited traps, light traps, oiled paper traps, or by spraying indoors with pyrethrum sprays and collecting the sandflies from a white sheet laid over the floor. Soil from possible breeding places was examined by flotation methods.

The following species were taken: *Phlebotomus argentipes* (3,227 ♀, 853 ♂), *P. antennatus* (27 ♀, 45 ♂) *P. babu* (?) (9 ♀, 4 ♂), and 1 ♀ and 6 ♂ of uncertain identity. *P. antennatus* had not previously been recorded from Ceylon and *P. zeylandicus*, common in parts of the main island of Ceylon, was not found on Delft Island.

P. argentipes, the predominant species, was more abundant in January than during July and August. They occurred in about the same densities during January in stone-and-mud houses and in those built of coconut palm leaves but they were more common in the stone-and-mud houses in the dry season (July–August). Males usually formed less than about 23 per cent. of the catches but in two instances much higher percentages (68 and 75·5 per cent.) of males were taken. Females, engorged apparently with blood, were caught during both the dry and wet seasons, but those with ripe ovaries were more numerous in the wet season.

Of 148 possible breeding places of *Phlebotomus* examined 19 were positive for immature stages of the fly. The positive sites were crevices in the floors and plinths of houses, the soil at the edges of refuse heaps and at the base of stone walls. In January, 18 out of 110 sites contained larvae, larval skins, or pupal cases and of the 38 sites examined during July and August only one, containing one pupa, was positive.

Breeding appears to be restricted in the dry season (July and August).

Captive females of *P. argentipes* deposited 95 eggs in the laboratory; the larvae which hatched from these eggs were bred out in moist soil and crushed guineapig faeces and 15 ♀♀ and 10 ♂♂ were obtained 28–35 days after the original oviposition. The temperature of the laboratory varied from 25° to 28°C. and the relative humidity from an afternoon mean of 66·6 per cent. to a morning mean of 74·4 per cent. The temperature of the breeding medium at one inch below the surface was consistently 30°C. *D. S. Bertram*

LUSCHER, M. **Continuous Observation of Termites in Laboratory Cultures.** *Acta Tropica*. Basle. 1949, v. 6, No. 2, 161–5, 2 figs.

The author describes a technique which he has employed successfully for maintaining colonies of termites in captivity and under conditions in which constant observations can be made.

One wall of the nest consists of a clean photographic plate (12 × 9 cm.). The other wall is made in sections with ordinary microscopic slides, the slides being separated from the plate by narrow glass slips arranged to form the sides, bottom and top of the nest. The thickness of the glass slips is only sufficient to give the termites room to move freely between the plate and the slides. The space allowed varies with the species of termite but it is between 1·5 and 4 mm. The lower quarter of the nest is partly cut off from the rest of the chamber by two transversely arranged glass slips. These, however, do not meet in the centre, thus leaving a communicating gap between the upper and lower compartments. The lower chamber contains damp cotton wool. Glass wool plugged into the central gap draws up the water and maintains a high humidity in the nest proper. The termites, together with fine clean sand and selected wood, are accommodated in the upper compartment. All junctions of the glass slips, the plate and the slides are sealed with wax except at one point where a small crack is left open for aeration.

Nests of *Calotermes flavicollis*, *Reticulitermes lucifugus*, *R. hesperus* and *Zootermopsis angusticollis* have been maintained in a healthy reproductive state for up to fourteen months.

Replenishment of the water in the wool is necessary every four to six weeks. This is accomplished by removing the slide overlying the wool. As the slides

covering the nest become obscured by accumulating débris and faeces they are removed and replaced by new slides.

Apart from observations on the termite castes and so on, these nests have been useful for extensive tests on the resistance of different woods to termite attacks. *D. S. Bertram*

SAUTET, J.; LEVAVASSEUR, G.; VUILLET, J.; ARDOIN, R. Possibilités d'action directe et indirecte des ultrasons dans la lutte antilarvaire contre le paludisme, la fièvre jaune et la dengue. Première partie. Action biologique des ultra-sons sur les culicides [SAUTET, LEVAVASSEUR & VUILLET]. [**The Possibilities of controlling Malaria, Yellow Fever and Dengue by the Direct and Indirect Action of Supersonic Waves on Mosquito Larvae.**] *Rec. Travaux Inst. Nat. Hyg.* Paris. 1949, Tome 3, v. 3, 997–1020, 17 charts & 3 figs. Deuxième partie. Action des suspensions de D.D.T. et autres corps traitées par les ultra-sons [SAUTET, ARDOIN, LEVAVASSEUR & VUILLET]. [**The Action of Suspensions of DDT and other Substances Irradiated by Supersonic Waves.**] *Ibid.* 1021–8.

In the first paper the authors have investigated the effectiveness of supersonic waves for the destruction of the eggs, larvae and pupae of some culicine mosquitoes and of *Anopheles maculipennis*. Under experimental conditions in which the impact of the waves on the organism is ensured for the whole of the exposure period death may follow immediately or after a period of a few hours. Immediate deaths are caused in late larval stages by evisceration whereas, in the young stages, the tissues of the larvae are disintegrated. Eggs are ruptured by effective treatments. Some eggs which survived treatment gave rise to larvae which developed more rapidly than control larvae. Exposures to 1,200 mÅ for two seconds or to about 300–400 mÅ for thirty seconds are effective but this effectiveness varies somewhat with the stage and the species of mosquito.

In experiments in which the waves were not evenly reflected throughout small breeding dishes of about one litre capacity some larvae died immediately but others survived for up to seven days even after 10–15 minutes exposure of the water to 1,200 mÅ.

Moulting, pupation and the emergence of adults follows after inadequate treatments.

There is little indication that the type of apparatus employed (this is described and figured) is likely to be of practical value for the control of mosquitoes under field conditions.

The second paper deals with a few small experiments on the effectiveness of DDT, pyrethrum and hexachlorocyclohexane (benzene hexachloride) against culicine larvae. Only five larvae were used in each experiment. Irradiation with supersonic waves is an added factor in some of the tests but it is not, in the reviewer's opinion, clearly shown that this materially improves the action of the insecticides. *D. S. Bertram*

LABORATORY PROCEDURES

COUDERT, J. & JUTTIN, P. A propos des méthodes d'enrichissement des selles. [**On Methods of Enrichment of the Stools.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 3/4, 111–14.

The authors find that direct examination of the stools is often insufficient and that some enrichment method is necessary. The essential conditions for such methods are that :—

(1) A large number of parasites should be concentrated in the least possible volume ;
(2) the maximum amount of inert matter should be eliminated ;
(3) the morphology of the cysts and ova should be maintained.

Several methods in common use are discussed. The method of CARLE and BARTHÉLÉMY (1913) takes too long and entails the use of two reagents. Further, the formalin alters the shape of cysts. The method of YORK and BIDEGARRY gives good results but has the same disadvantage of being long and in addition requires a 30 per cent. solution of saccharose, a material difficult to obtain at present.

The method of TELEMANN modified by Garin eliminates some of the disadvantages of the former of the above methods. The technique that the authors suggest is a modification of this method : it is as follows :—

A " walnut " of faeces is added to 100 ml. of water. The solid matter is pulverized with an agitator and a fine emulsion obtained. The material is allowed to settle for one minute. In an ordinary centrifuge tube are placed 5 to 6 ml. from the superficial layer of the emulsion and 1 ml. of hydrochloric acid is added : the whole is shaken : 2 or 3 drops of toluene are added and the preparation is again shaken vigorously : the tube is filled with ether : the whole is shaken and centrifuged slowly for 3 or 4 minutes.

The sediment is examined between a slide and coverslip.

The order in which the materials are added is important.

The method has been used for 6 months in the *Laboratoire de Parasitologie de Lyon* and over 500 stools have been examined. It was found very satisfactory even in the examination of icteric stools which usually present difficulties.

L. E. Napier

PICK, F. Nouveaux dispositifs pour la technique de la coproculture. [**New Methods of Coproculture.**] *Acta Tropica.* Basle. 1948, v. 5. No. 4, 354–7, 4 figs.

Pick describes and illustrates some new methods of recovering nematode larvae from faecal cultures. These are modifications based on the principle involved either in the Baermann technique or on the Petri dish technique and as they require a minimum of laboratory apparatus are useful in routine examinations. The illustrations should be seen in the original.

J. J. C. Buckley

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

COLONIAL OFFICE. **Colonial Research 1948–49. Reports of the Colonial Research Council, Colonial Products Research Council, Colonial Social Science Research Council, Colonial Medical Research Committee, Committee for Colonial Agricultural, Animal Health and Forestry Research, Colonial Insecticides Committee, Colonial Economic Research Committee.** Cmd. 7739. 134 pp. 1949. London : H.M. Stationery Office. 2s.]

This Report comprises 7 sections, each an annual report (1948–49). The bodies represented are : Colonial Research Council ; Colonial Products Research Council ; Colonial Social Science Research Council ; Colonial Medical Research Committee ; Committee for Colonial Agricultural, Animal Health and Forestry Research ; Colonial Insecticides Committee ; Colonial Economic Research Committee. Of these, the reports of the Colonial Medical Research

Committee, and the Colonial Insecticides Committee will be of most interest to readers of this *Bulletin*.

The list of schemes approved in the financial year 1948–49 for grants under the Colonial Development and Welfare Acts is most impressive. The sum covered in this list is £1,652,169, and the allocations made since the inception of the organization after the first Act of 1940 have reached the figure of £5,913,795. The actual issues in relation to the research schemes (many of which are planned to extend over several years) are, of course, much less, £1,539,416, but the money for the remainder is available and in due course the work which it represents will be accomplished. Medical research is well represented in this list, but no individual item commands the big sums given to certain projects of fishery research and of agriculture and forestry research. Nevertheless, there are many medical projects of considerable size, and very varied interest.

The East African Medical Survey, now begun in Tanganyika Territory, should provide useful information on the vital statistics and common diseases of the Africans living under rural conditions, provided that it is carefully carried out for a long period. Some readers will remember the survey conducted in the Kahama district 20 years ago by Dr. A. R. Lester, which was abandoned when it became evident that the outbreak of trypanosomiasis was interfering grossly with the Africans and their cattle ; it is to be hoped that this history will not be repeated.

The virus research laboratories in Uganda and Nigeria are to be taken over completely from the Rockefeller Foundation (which has partly financed them) in the near future, and the laboratory at Freetown will be taken over from the Liverpool School of Tropical Medicine. The staffing of these laboratories has presented difficulties, but when these are surmounted there should be opportunity for much fundamental research. Apart from these there were several projects in being : the Nutrition Research Station in the Gambia, where improved methods of farming are being tried, research on malaria in North Borneo, Malaya and East Africa, on scrub typhus in Malaya, relapsing fever in Kenya and on physiology in Uganda and Nigeria. The Report itself is much more than a catalogue of these efforts, in that it gives considerable detail of some of the work. For instance, the recommendations on dosage of proguanil (paludrine), made by the team working on a West African strain of *P. falciparum* at Horton, are given in full, and there is much detail of the results obtained in the treatment of schistosomiasis with Miracil D, and of scrub typhus and typhoid fever with chloromycetin. Similarly, the investigations into transmission of yellow fever in Uganda and scrub typhus in Malaya are summed up (so far as they have gone) in such a manner that an administrative officer could obtain a reasonable grasp of the subjects. These accounts add very greatly to the interest and value of the Report.

The Report of the Colonial Insecticides Committee is equally interesting, reference being made to the mosquito eradication experiments in Cyprus and Mauritius, to the various malaria experiments and to the work being done against tsetse and other flies. Some of the work of this Committee and of the Colonial Insecticide Research Unit, Uganda, is concerned with agricultural problems. *Charles Wilcocks*

COMMONWEALTH INSTITUTE OF ENTOMOLOGY. **Report of the Fifth Commonwealth Entomological Conference 22nd–30th July 1948.** pp. ii+112. 1948. Dec. London : 41, Queen's Gate, S.W.7. [7*s*. 6*d*.]

Forty-six delegates and official observers attended the Fifth Commonwealth Entomological Conference held from the 22nd to the 30th July, 1948, in London.

The formal Report includes a list of the delegates and observers; the opening address by Col. J. G. ROBERTSON—who reviews the history of the Commonwealth Institute of Entomology since its creation in 1913 as the Imperial Institute of Entomology—and a number of conclusions and resolutions passed by the Conference affecting editorial policy for the *Review of Applied Entomology* and the *Bulletin of Entomological Research*; the organization of biological control in the Commonwealth; the expansion of termite-research and the preparation of a manual on anti-termite measures; the nomenclature of modern insecticides; the setting up of an African Phytosanitary Convention; research on infestations of stored products; and the training of entomologists. It is recommended that some future conferences should be held outside the United Kingdom and that the Sixth Conference should be planned for 1953.

Then follow three Appendices: Appendix I gives an account of the work of the Institute from 1935 to 1948; Appendix II is concerned with the proceedings of several committees, many of whose deliberations are embodied in the resolutions of the Conference; Appendix III, which comprises some 85 out of the total of 112 pages of this publication, records the scientific discussions held during the week.

In *Recent Developments in Insecticides*, GALLEY reviews developments since 1942; he comments briefly on DDT and benzene hexachloride (BHC) and deals more fully with the chemical constitution, use and limitations of, among others, Chlordane (= "Velsicol 1068", "Octaklor"), Toxaphene (chlorinated camphene), phosphorus compounds such as "Bladan" and E.605 (=Parathion; 3422, Thiophos), and the systemic insecticides containing flourine or flourine and phosphorus. The high toxicity of some of these newer insecticides to mammals (possibly 70–100 times as high as DDT) has stimulated work on synergists for pyrethrum, *e.g.*, piperonyl butoxide and piperonyl cyclonone, and studies on chemically constituted "hybrids" of pyrethrin and DDT. In *The Mode of Action of New Insecticides*, WIGGLESWORTH considers the problem from three different aspects: the manner in which an insecticide is picked up by an insect; the route of its entry into the insect; and its action on the physiological processes of the insect. Examples illustrating each aspect are drawn mainly from the evidence available for DDT. The session on the *Uses and Limitations of the new Insecticides in the Field* brings out that the urgent need for new insecticides particularly concerns agricultural and horticultural interests. Benzene hexachloride, which has good acaricidal properties, is limited in its use for edible plant products on account of a musty flavour which may persist in raw, cooked and canned fruits and vegetables even if, in some cases, the treatment preceded harvesting by 60 days (peas) or 44 days (plums). Potato tubers were inedible when harvested from soil treated about a year previously with 7·5 lb. crude BHC per acre. Provided the tainting powers can be satisfactorily eliminated from this compound, it has useful applications in pest control. Certain of the newer substances are promising acaricides and others have ovicidal properties. It is clear from this and other discussions that toxicological problems raised by residual insecticides like DDT and benzene hexachloride and by some of the phosphorus compounds which are absorbed and retained by treated crops, are receiving close attention. *Recent Developments in Pest and Disease Control Machinery*, by KEARNS, is concerned with advances in the design of heavy mobile equipment and auxiliary apparatus for use against agricultural and horticultural pests. Experimental work is in progress on equipment for the dispersal of concentrates by compressed air expansion, but washes and dusts are likely for some time to remain the general methods for practical application of insecticides in this field. The discussion by GUNN on the *Application of Insecticides from the Air* compares the Porton, high-level flight, method and the low-level flight "cloud" method of dispersing insecticides

from aircraft. Besides considering the special difficulties associated with aerial spraying *per se*, the speaker examined each method as regards its characteristics for droplet size, homogeneity of deposit, cost, and so on and its general suitability for different types of terrain, vegetation, and pests. There is information as to the relative cost and practicability of helicopters and fixed wing aircraft. The several contributions on *Biological Control* [BAIRD, CATTIER, LEPELLEY and MILLER] include a general account of the wide scope of work undertaken at the Commonwealth Bureau of Biological Control in Canada, and a review of successful control by biological methods of *Pieris rapae* (a pest of cruciferous crops) introduced into New Zealand in 1929, and of the mealybug (*Pseudococcus kenyae*) of coffee introduced into Kenya from Uganda. There is a discussion on the use of phytophagous insects for weed control. The advantages of a central institution in the Commonwealth for the co-ordination of research, information and supplies of predators and parasites for biological control is clear from the discussion. The chapter on the *History of the Bureau of Biological Control* (now at Belleville, Canada) makes complementary reading. *The Developments in the Control of Stored Products*, reviewed by RATCLIFFE, received particular stimulus during the war. In Australia, with regard to wheat, particular attention is paid to the acceptance of suitably dry grain ; DDT and BHC are in restricted use on account of possible toxicity risks. Elsewhere, storage bags impregnated with DDT (1–5 per cent. by weight) have been found effective in controlling infestations of different commodities by various pests. There is, however, considerable absorption of the insecticide by fatty commodities, *e.g.*, flour, groundnuts, and soya flour, stored in treated bags. The discussion also raises the possibility of controlling timber beetles by means of the new insecticides which are absorbed and retained by plants. The opening papers by NASH and MORRIS and subsequent discussion on *Tsetse Research and Control* review the varieties of environment and terrain suited to different species of tsetse fly and discuss various methods employed for their control, in some instances for their eradication, in West and East Africa, Rhodesia and Zululand. Other subjects mentioned in the course of this session are : the use of insecticides against tsetse fly ; the elimination of a residual tsetse population by introducing alien male flies ; mosquito breeding in clearings ; selective clearing by mechanical means or by plant poisons ; radioactive salts for " marking " tsetse fly ; mass prophylaxis and mass chemotherapy of sleeping sickness. The discussion on *Locusts and Grasshoppers* [UVAROV and NICHOLSON] considers the relative merits in control of direct defence (*i.e.*, the destruction of established swarms by insecticides or baits), outbreak suppression (*i.e.*, the detection and destruction of incipient swarms in known " outbreak areas " where the solitary phase transforms into the gregarious phase) and the prevention of swarming (*i.e.*, the prevention of swarming in outbreak areas by inducing fundamental changes in these ecological conditions presumed to initiate phase transformation). The section on the *Estimation of Insect Populations in the Field* by STRICKLAND is non-mathematical ; it reviews briefly, but informatively and critically, the efficiency of a great variety of methods and devices for sampling field populations of vectors, pests, and parasites of medical, veterinary, agricultural or horticultural interests. *The Summary of Information on Termites* derives from a resolution by the Fourth Conference in 1935 to compile a report on termite damage and control within the Commonwealth. The report indicates in considerable detail the nature of the damage done in various countries under such headings as growing crops, stored timber, poles and fencing, and buildings. Nest destruction and various methods of protecting and repairing buildings and of dealing with stored timbers, including the use of structural devices and preservatives, are described. The availability of termite-resistant

indigenous timbers is recorded. There is need, it is noted, for entomologists to study the taxonomy of termites and to combine this with field studies and for fundamental research on termite colonies under laboratory conditions. It is thought that insufficient use has been made up to the present of those anti-termite measures known to be efficacious.

[This report as a whole is an invaluable guide to recent advances in applied entomology; it constitutes a review of those fundamental researches and practical developments which have taken place during or since the recent war and many of which have hitherto not been widely appreciated owing to security restrictions and other considerations affecting the rapid and general publication of reports. Containing, as it does, a wealth of information and authoritative opinion on many topics, it is a timely and welcome publication.]

D. S. Bertram

British Commonwealth Collections of Micro-Organisms. **Directory of Collections of Micro-Organisms maintained in the United Kingdom and Crown Colonies.** 1949, May, Issue No. 1, 27 pp.

Laboratory Animals Bureau. **Catalogues of Arthropods, Helminths, Molluscs and Protozoa of Interest to Medical and Veterinary Workers.** 1949, May 9, 25 pp. cyclostyled. London: Royal Veterinary College, Royal College Street, N.W.1. [Summary appears also in *Bulletin of Hygiene.*]

A Committee, set up by the British Commonwealth Scientific Conference in 1946, to consider the extent of the field to be covered by type culture collections, recommended that this subject be referred to a specialist conference which met in August 1947. This specialist conference discussed, among other matters, the best way of keeping institutes throughout the Commonwealth in touch with developments in the United Kingdom in relation to type cultures.

The present "Directory of Collections of Micro-Organisms maintained in the United Kingdom and Crown Colonies" is one outcome of their deliberations. It gives an alphabetical list of 188 collections with the names of the scientists in charge, and notes of the interests served, the types of organisms maintained, and the conditions of supply to applicants. The main types of organisms, listed only in general terms, include algae, animal and plant pathogens, bacteria, fungi, yeasts and industrial ferments, marine, soil, water and sewage organisms, and protozoa. Only two of the 188 collections noted are maintained in the Crown Colonies, viz., the West African Cacao Research Institute, Gold Coast, and the Hankey Culture Collection, Trinidad. It is hoped later to publish a detailed list of the genera and species kept in the collections.

Similar information, but in this case relating to invertebrate animals concerned in the transmission of disease, has been compiled by the Laboratory Animals Bureau of the Medical Research Council, and is made available in the "Catalogues of Arthropods, Helminths, Molluscs and Protozoa of Interest to Medical and Veterinary Workers" now issued in cyclostyled form. These Catalogues give in List I the general information as to numbers and types of organisms maintained at some 25 institutes in the United Kingdom, with names and addresses of persons to whom application may be made for specimens, and in Lists II A, B, C & D, relating respectively to Arthropods, Helminths, Molluscs and Protozoa, the more detailed information including the generic and specific names of parasites or vectors, names of hosts in which maintained, mode of transmission, and history of strains, with the code numbers of institutes where they are to be found.

The "Directory" is available free on request from the Secretary, United Kingdom National Committee of the British Commonwealth Collection of

Micro-organisms, 38, Old Queen Street, Westminster, London, S.W.1, and the "Catalogues" are available free on request from the Director, Laboratory Animals Bureau, Royal Veterinary College, Royal College Street, London, N.W.1.

It is recognized that the particulars so far collected are probably incomplete, and institutes which are maintaining cultures and are willing to co-operate are asked to send details of their collections to the appropriate address for inclusion in future lists. *R. L. Sheppard*

INDIA. **Annual Report of the Public Health Commissioner with the Government of India for 1946** [MEHTA, J. N., Director General of Health Services, Govt. of India]. 117 pp., 1 folding map. 1948. Delhi: Manager of Publications. [*Rs.* 2–12 or 4*s.* 6*d.*]

This Report, dated November, 1947, is signed by Dr. Jivraj N. Mehta who was the first Director General of Health Services of the new Government of India established in August, 1947. It closely resembles the report for 1945 except that the Arms of the new Government on the cover replace the Royal Arms.

The only statistical table that is provided deals with the birth, death, and infant-mortality rates of the parts of India still described as British India. These statistics have always been regarded as quite untrustworthy for most of the Provinces, and in view of the disturbed conditions prevailing in 1946 they are not likely to be any more reliable than formerly. Startling variations occur in the figures for different Provinces; for example the birth rate is shown as 18·0 in Sind and 37·7 in the adjoining Province, Punjab; the death rate is shown as 8·7 in Sind and 26·9 in Central Provinces. For what they are worth the figures suggest that the birth rate has risen appreciably from the low rates recorded during the years 1942–1945.

In the body of the Report figures are given for three rural areas in which experimental Health Units have been working for several years; these figures are likely to be fairly reliable because the reporting agents have been under supervision of the staffs of the Units, and although they deal with small samples of the population—about 50,000 each—they are significant in showing what has happened in typical areas provided with a modest health organization. If similar results were to follow the establishment of such Units throughout India the rate of growth of population would be greatly accelerated.

	Birth Rate		*Death Rate*		*Infant-Mortality*	
	1946	1945	1946	1945	1946	1945
British India	28·9	27·3	18·4	21·5	135·8	150·9
Najafgarh Health Unit (Delhi Province)	45·7	48·6	17·5	24·0	110·7	151·7
Singur Health Unit (Bengal) ...	42·5	—	16·5	—	126·3	—
Poonamallee Health Unit (Madras Province)	36·3	22·7	21·9	25·5	166·2	240·8

The only reference to the population problem in the present Report is the following statement by Dr. Mehta in his introductory remarks: "During recent years India has gradually drifted into a position of food scarcity. The pressure of the increased population on the land is only one of the factors creating such a situation."

This statement should be read in conjunction with remarks contained in the section on Nutrition from which it appears that food rationing was in force for 130 millions of the people and that the daily adult ration provided barely 1,200 calories—"possibly the lowest intake of rationed foods in the world." The total production of cereals in India is said to be 4,000,000 tons yearly, the

quantity needed being about 8,000,000 tons; the shortage was partly made up by importing 2,000,000 tons "and this was all that was available."

These statements suggest that to maintain the people of India in a moderate state of nutrition the food supply would have to be twice as great as the amount actually being produced in India, and that even if this huge increase could be made available a further progressive increase would be needed for the rapidly growing population.

The most authoritative pronouncement on this appalling problem has been made by the Health Survey and Development Committee in their Report, dated 1946 [which was reviewed at length in this *Bulletin*, 1947, v. 44, 252].

This problem of population and food supply is by far the greatest of all public health problems not only for India but also for most of the countries of the world. Competent experts have estimated that one-half of the world population are suffering from severe malnutrition and that one-half of the rest are undernourished.

Public health workers everywhere, except in a few progressive countries are faced with a situation in which their efforts to improve health conditions, must inevitably fail unless a suitable balance can be established between the number of mouths to be fed and the food that is available. A tragic feature of the situation is that the more lives are saved by the control of infectious diseases the sooner will the food-supply position become acute.

It may be argued that population control and food production are not subjects for which health organizations are responsible, but although this is technically true it would be a suicidal policy to remain silent and inactive spectators of the process of undermining the very foundations of the public health structure.

What can be done is to make the problem a subject of study in every public-health curriculum and to organize a concerted effort to arouse both governments and peoples to a sense of the gravity of the situation and of the need for action to avert disaster.

No apology is needed for calling special attention to the above problem; the rest of the Report is relatively unimportant, it deals chiefly with the incidence of the great infectious diseases, none of which was unusually prevalent in 1946.

Cholera was less severe than in 1945, though some readers may be surprised by the statement that in Bengal "the incidence of the disease was even milder this year" when they go on to read that there were 27,710 deaths. Cholera inoculation was extensively carried out; in Bengal nearly 8,000,000 persons were inoculated.

Plague was epidemic in some parts of the United Provinces where there were 18,199 deaths, also in Bombay, Bihar and Madras.

Malaria was severe in Bihar, but not in any other province. Plans were made during the year for controlling the disease by DDT and paludrine [Proguanil].

Tuberculosis received special attention; reference is made to proposals to employ BCG vaccine as a control measure.

Leprosy treatment and control on comprehensive lines was being planned in Bengal.

Kala azar was not specially prevalent in any province; the only figures given are for Assam where 22,000 patients were treated.

At a Conference of the Provincial Ministers of Health the recommendations of the Health Survey and Development Committee were accepted in principle as "objectives to be kept in view," but the programme for the first five years was regarded as "not within present financial resources."

A brief summary is given of the valuable research work carried out during the year; the chief subjects were malaria, nutrition, cholera, plague, and leprosy.

The activities of the voluntary health organizations are described; these include the Red Cross and St. John Ambulance organizations, the Tuberculosis Association of India, the British Empire Leprosy Relief Association (India Council) and various provincial Maternity and Child Welfare Associations.

John W. D. Megaw

LOURENÇO MARQUES, MOÇAMBIQUE: Missão de combate as tripanossomíases. Relatório anual de 1947. [**Mission for combating Trypanosomiasis. Annual Report for 1947.**] 132 pp. 11 maps, 3 graphs & 1 plan. [10 refs.] 1948.

The Mission was appointed in 1945 and its field of action is practically the whole Colony of Mozambique; the construction of the hospitals, dwelling-houses and other works is expected to be completed by June, 1949. The Chief of the Mission, Dr. Mario Augusto de Andrade e Silva, succeeded his predecessor Dr. Jacinto de Sousa on 1st April 1947. The Staff consists of 45 Europeans and 103 Africans; the former include 11 medical officers, 5 veterinary surgeons, a botanist, and an entomological staff of 14 under the direction of Mr. H. E. Hornby, formerly the Director of Veterinary Services in Tanganyika Territory. The expenditure during 1947 was 6,298,699 escudas [about £63,000 at 100 escudos=£1].

The regions of the Colony where the Mission worked were divided into 9 medical sectors and 4 veterinary sectors; the former are all north of the Beira-Mashonaland railway, 5 being in Niassa province and 4 in the province of Manica and Sofala which borders on Northern and Southern Rhodesia. The 4 veterinary sectors occupy the whole of the southern part of the Colony from the Natal boundary to the Zambesi river; on the west they border on Swaziland, the Transvaal [the Kruger National Park] and Southern Rhodesia.

Inspection.—During the year Dr. de Andrade e Silva toured the Colony with Dr. F. Pires, the chief veterinary officer of the Mission or with Mr. Hornby, or with both, and inspected most of the sectors; a short description of these journeys is given.

Tsetse fly surveys.—The distribution of the 4 species of tsetse fly—*Glossina morsitans*, *G. pallidipes*, *G. brevipalpis* and *G. austeni*—found in the Colony, is shown on several coloured maps, and brief notes of the position in the various districts are given in the text. *G. morsitans* infests most of the area from the River Rovuma (the northern boundary with Tanganyika Territory) to about 40 miles south of the River Save; *G. pallidipes* is widely spread in the provinces of Niassa and of Manica and Sofala; *G. brevipalpis* and *G. austeni* are shown in the eastern part of the *G. morsitans* area and also in the Maputo river region south of Lourenço Marques. In November 1946, Hornby surveyed the western part (Alto Limpopo) of the country between the Save and Limpopo rivers and concluded that, owing to the climatic conditions, the kind of vegetation, and the distribution of the game animals, *G. morsitans* could not easily invade this area [see this *Bulletin*, 1948, v. 45, 584]. His findings were confirmed by an aerial survey made by the botanist, the assistant entomologist and Dr. Pires in November 1947. Other surveys by Hornby included one of the east coast south of the River Save where conditions favourable to tsetse flies, especially *G. morsitans* and *G. pallidipes*, were found; preventive measures will be taken in this area (Govuro) in 1948. Another survey was in the Maputo district between Lourenço Marques and the Natal boundary [see this *Bulletin*, 1948, v. 45, 1068].

Sleeping sickness.—This is practically confined to the two provinces of Niassa and Manica and Sofala and nearly all the cases in the latter province occurred in the Tete district. There were 253 cases (4 in Europeans), 197 in Niassa province and 56 in the Tete district, an increase of 101 on the number (152) in 1946. The incidence was 1·2 and 0·7 per 1,000 of the population respectively and the highest local incidence was 4·3 per 1,000 in Moçimba da Praia in the extreme north. The population is mostly scattered in the bush in small groups of one or two families, which is unfavourable to the occurrence of epidemics, and the chief cause of the increase of the disease is the movement of people due to the great increase in agricultural and industrial labour. There are 8 hospitals and 13 (later 26) observation posts. Patients are treated with antrypol and tryparsamide. The usual prophylactic measures of mass examination of people, bush clearing, disinfestation of vehicles and travellers on roads, were taken and 1869 prophylactic injections of antrypol were given.

Animal trypanosomiasis.—The veterinary sectors were determined by the need to protect cattle from nagana in some parts and by the importance of other areas for animal husbandry. It was necessary to protect the Sul do Save province (south of the Save river) as it has the best conditions for the cattle industry and is the least infested by tsetse flies. Sector 1 (H.Q. Maputo) has splendid resources for cattle breeding ; in Sector 2 (H.Q. Mambone at the mouth of the River Save) the right bank of the River Save and the area of Govuro must be kept under observation in regard to *G. morsitans* ; Sector 3 (H.Q. Espungabera on the Southern Rhodesian boundary opposite Melsetter) between the Rivers Save and Lucite, is heavily infested with tsetse flies but has agricultural importance ; and in Sector 4 (H.Q. Vila Péry on the Beira-Mashonaland railway) the largest European settlement in the Colony is established and a high proportion of the cattle are infected with nagana.

The nagana problem is very serious and is the greatest obstacle to the future economic and social development of the Colony ; nearly two-thirds of the Colony is infested with tsetse flies and nagana occurs also in some parts where no tsetse flies have been found, and it is thought that mechanical transmission may be important. There are about 600,000 head of cattle of which 450,000 live south of the River Save, 100,000 in Manica and Sofala, 30,000 in Zambesi province and about 4,500 in Niassa province. The corresponding approximate figures for sheep are 30,000, 20,000, 4,500 and 4,000 ; for goats 75,000, 90,000, 9,000 and 90,000 ; and for pigs 20,000, 28,000, 4,500 and 4,500. These are shown on a graph. In the province of Sul do Save very few cattle belong to Europeans, from lack of interest, but this area is very favourable for animal husbandry. Except in the provinces of Sul do Save and Manica and Sofala (Angónia) the Africans do not keep cattle. Most of the cattle in the provinces of Zambesi and Niassa belong to large agricultural companies and in spite of periodic treatment of infected animals these companies have to import cattle to make up their losses.

The commonest species of trypanosome in cattle, sheep and goats is *T. vivax* ; next comes *T. congolense*, then mixed *T. vivax* and *T. congolense*, while no *T. brucei* were found in 31,888 animals examined. *T. simiae* was found in 5 pigs.

The Maputo region is very important ; it has an equable climate, rich pasturage, fertile soil, and the valleys have abundant water for irrigation. It has been reported on by the veterinary officer of the Mission and by Mr. Hornby [this *Bulletin*, 1948, v. 45, 1068]. The only tsetse flies found are *G. brevipalpis*, near the River Maputo, which feeds chiefly on hippotomus, cattle and small antelopes, and *G. austeni*, near the Libombos to the west where game is abundant. The right bank of the Maputo river is a reserve of elephants of which there are over 2,000 ; there are also 6,000 head of cattle in this reserve

and these should be kept separate from the game by a strong sisal hedge. In 1948 the Mission will try the effect on *G. brevipalpis* of applying DDT and gammexane to the cattle. The phenanthridinium compound M & B 1553 was given to 496 head of cattle and a month later hardly any showed *T. congolense*, and all increased in weight. A list of other biting flies and ticks is given.

In the Govuro region near the River Save, where there is a high rate of infection, the cattle of the Europeans were treated with dimidium bromide, a phenanthridinium compound, and in 1948 the Mission will treat all the native cattle with this drug. In Machanga on the left bank of the Save most of the cattle belong to the Africans and are in poor condition and short of grazing areas. In the Chimoio region the Europeans are chiefly interested in cattle for work on their farms ; in 1945 there were 13,432 cattle, all imported from the Tete region ; they are underfed and overworked and about 80 per cent. suffer from nagana. No tsetse flies have been found in the area but in 1948 a survey with Harris traps and animals as bait will be made. The Muda region is important from its nearness to Beira ; the plains near the River Pungwé, 60 km. from Beira, could support some thousands of cattle. Repeated searches failed to find tsetse flies until Dr. Pires found *G. morsitans* in June 1947. Anti-tsetse measures would be relatively easy and cheap. The region is very important for the future development of Beira. The Mossurize area has conditions very favourable for European agriculturists ; the present African population is too small and the position should be reviewed. It is near the progressive district of Melsetter in Southern Rhodesia. The tsetse situation here is very serious. In the Tete region the periodical bad condition of the cattle is largely due to the shortage of water and pasture owing to over-concentration of the cattle near the permanent rivers. Tsetse flies cannot establish themselves here but occasional contact is possible. The Zòbué region, near Tete and contiguous with Nyasaland, has exceptionally good conditions for agriculture and animal husbandry ; its average altitude is 900 metres, its climate is agreeable, the soil is fertile and water is abundant. This area and the adjoining one of Angònia should supply the neighbouring coal mines of Moatize and future local industries with agricultural products.

The author advises that priority should be given to those regions with the most urgent need or which have the greatest economic importance—Maputo, Govuro, Muda and Tete.

Tsetse control.—Maputo region : Hornby studied the breeding grounds and resting places of *G. brevipalpis* and began an experiment in control based on clearing. A tractor cleared one hectare [about 2½ acres] per hour, which is about equal to the work of 200 labourers ; the cost was 43$ 80 [say 10/-] not counting European supervision. The results of searches for flies and pupae during the next half year or more showed that it is possible and economical to control *G. brevipalpis* in Maputo either by settlements protected by peripheral clearings or by discriminative clearing.

Mutuali region, in Niassa province : The Centre for the Scientific Investigation of the Cottontree needed protection from sleeping sickness for the workers ; clearing, hunting of game, traffic control and resettlement of natives of sleeping sickness foci were carried out, measures which are described in some detail. The results were good and the development of the area should be continued.

The game problem.—The Colony has enormous numbers of wild animals including many thousands of elephants and buffaloes, which have recently greatly multiplied. The author discusses the question thoroughly. Much damage to farms is done, game is a reservoir not only of trypanosome diseases but also of several other fatal diseases of domestic animals, but there are strong reasons for preserving it. The interests of the people should be

paramount and game should be killed in regions with agriculture and cattle, but should be protected in reserves and national parks where economic development is not interfered with. A fresh-water fish industry should be developed as a valuable source of protein food.

The Report is an interesting record of much valuable work; the coloured maps are most helpful to the reader. *J. F. Corson*

GALLIARD. Considérations sur la parasitologie. [**Reflections on Parasitology.**] *Rev. Paludisme et Méd. Trop.* 1949, June 15, v. 7, No. 61, 153–63.

This is an abbreviated account of the lecture that the author gave to the Faculty of Medicine of Paris on his inauguration to the chair occupied for 30 years by his famous predecessor E. Brumpt. It is a review of the modern trends of the subject, coloured by the rather special outlook of the Paris School. He first shows how inaccurate is the idea that morphology has had its day, illustrating this by the example of the importance of minute sub-divisions of anopheline species in malariology, where on a number of occasions these details have provided the final clue to a problem. He is not a rigid systematist, however, *e.g.*, he fully recognizes the importance in medical practice of different strains of the species of plasmodia, filaria and other helminths, and is willing to relax the laws of nomenclature in order to define these strains by special names. Much of the lecture was devoted to problems of immunity; the divergent ideas on this subject were shown to be due to various causes, *e.g.*, the existence in different regions of biotypes showing different degrees of adaptation, the rôle of nutrition, etc. Chemotherapy has made immense strides, although it has often had a special difficulty to overcome, namely, the inaccessibility of the parasite to the drug, whether an adult filarial worm or an exo-erythrocytic schizont. In the preventive field, DDT offers immense possibilities; it is stated that after its use in Italy there was not a single death from malaria in 1948, the first year without such a death for 23 centuries.

Throughout his paper, wherein the author modestly refrains from any mention of his own not inconsiderable contributions, he emphasizes the importance of the parasitized person rather than the disease itself.

P. C. C. Garnham

REED, J. G. **General Report on the Health of the Estates of the District [Batang Padang, Perak, Malaya] for 1946, 1947 and 1948.** 11 mimeographed pp. 1949, Mar. Sungkai, Malaya.

This report on the health of a group of estates in the Batang Padang District of Malaya for the years 1946, 1947 and 1948 is of interest as a glimpse of changing conditions in the health of labour forces. The total population was 9,615, of whom 6,836 were Indians, the vital statistics referring to this last group. Since the war the births have increased greatly from a previous normal of about 38 per 1,000 to 61·3 in 1947, and 52·4 in 1948. The death rate has shown a steady decline since the war to 5·3, but in the absence of any figures on the age situation of the population this is difficult to interpret. The infant mortality rate has fallen to a low record of 87 per 1,000 live births. In common with the rest of Malaya, malaria has shown a marked steady decrease, the spleen rate in children falling in three years from 35·3 to 4·3 per cent. The explanation for this is not clear; it does not appear to be due to the use of suppressive drugs and the arguments in favour of increased immunity are weak; it would appear to be associated more with changing cultivation practices. On the other hand the nutritional state has not improved and the author considers that the root cause of sub-nutrition is certainly not solely economic as little improvement in the nutritional state accompanies improvement in the economic state. Education in feeding habits seems necessary. Anaemia

is markedly increasing and is becoming one of the most important causes of sickness and inefficiency, particularly among women. The report is accompanied by nine tables of statistics. *G. Macdonald*

PEÑA GARCIA, B. Comentarios sobre la labor realizada por el Laboratorio Clinico del Distrito La Salina durante el lapso 1938–1947. [**Analysis of Ten Years' Work at the Clinical Laboratory, La Salina, (Venezuela).**] *Bol. Med.* Caracas. 1949, Jan., v. 1, No. 2, 161–81, 1 graph. English summary.

This is a condensed account of the work carried out at the clinical laboratory of the Creole Petroleum Corporation's Medical Department at La Salina, Venezuela during the decade 1938–1947. The district concerned lies north-west of Lake Maracaibo. The employees and their families comprise 21,424 persons. During the period, 24,884 faecal examinations have been made and it is stated that "intestinal parasitosis is present in 8 out of every 10." The commonest, 32·8 per cent., is *Trichomonas hominis*, and next in order *Entamoeba coli* (32 per cent.), *Ascaris lumbricoides* (21·8), *Trichuris trichiura* (18·3,) *Chilomastix mesnili* (15·3), *Giardia intestinalis* (11·3), *E. histolytica* (4·5) and its cysts (4·3). Of 1,365 schoolchildren examined, 89·4 per cent. were harbouring parasites and 36·6 per cent. had more than one, the commonest being *Ascaris*. Cysts of *E. histolytica* were found in 6 out of 100 cockroaches (*Blatta americana*) examined and in 2 of the same number of flies (*Musca domestica*). *Malaria* is rife, but much less in the last four years, the morbidity per mille in the 5 years 1943–47 being 53·3, 28·8, 14·5, 14·1 and 7·9 respectively; the infection in 86·6 per cent. is by *P. vivax*. *Typhoid fever* is not common, but the number of cases, which in 1944 to 1946 were 6, 5 and 4 respectively, rose to 11 in 1947. All the proved cases occurred in parts "outside the sanitated sites." *Syphilis* which had been high, 73·4 per mille in 1943, fell to 43 in 1944 and in each of the next 3 years has been round 17 per mille. Smears of urethral discharge examined for gonococci numbered 4,890 and positive cases have tended to increase during the last 4 years, but "the examination is limited to direct examination of stained smears." *H. Harold Scott*

BOOK REVIEWS

SCHÖNHÖFER, Fritz *et al.* **Chemotherapy.** Fiat Review of German Science 1939–1946. 304 pp., 6 figs. 1948. Published by Office of Military Government for Germany, Field Information Agencies Technical, British, French, U.S.

This account of chemotherapeutic research in Germany during the war years is produced by the FIAT branch (Fie d Information Agencies Technical) of the Military Government of the British, French and U.S. Occupation Zones in Germany. It is a more polished production than the hastily prepared BIOS (British Intelligence Ob ectives Sub-Committee) reports, which served such a useful purpose a few years ago by giving the earliest possible publicity to available information on German scientific progress during the war. Unlike the latter production, the present one is a well-printed compact booklet, written not by the interv ewing teams who visited Germany immediately after the war, but by the German scientists themse ves. The senior author is Fritz SCHÖNHÖFER, and there are many other well-known names, such as those of DOMAGK, KIKUTH, MIETZSCH and MAUSS, among the 19 contributors.

Although the title page, the foreword (by the Chiefs of the three FIAT services), and the table of contents appear in English, the entire remainder of the volume is in German. It is in the form of 23 self-contained articles, well documented and with useful bibliographies. Where necessary, suitable reference is made to work carried out before the war leading up to particular developments described. There is an adequate author- and subject-index to the volume as a whole. The production is worthy of wider circulation than appears possible as yet, and we learn in the foreword that "The manuscript from which this volume has been derived has been turned over to a committee of German scientists which will make the arrangements necessary for printing other than this strictly limited edition. The latter is transmitted by the respective FIATs to their Government for distribution."

In his introductory note, SCHÖNHÖFER emphasizes the importance of close liaison between chemists and medical men if there is to be any substantial progress in the field of chemotherapy. And yet the element of chance continues to play a big rôle in the emergence of commercially successful preparations. Hardly a dozen such have arisen from the 20,000 compounds examined in 5 to 10 different types of animal test during the past 35 years in the Chemotherapeutic Laboratories of the *I.G.-Farbenindustrie* at Elberfeld.

The individual contributions are uneven in length and scope, but none is without some interest. The longest is a comprehensive account in 52 pages by PRIGGE of the experimental chemotherapy of tuberculosis and the biochemistry of the bacillus. Tuberculosis is also covered at some length, together with leprosy, in a contribution by WAGNER-JAUREGG. Then there are quite short articles, as for example a paper in 4 pages by KIKUTH on the sulphonamide treatment of virus infections, in which special reference is made to the suitability for laboratory investigations, of the broncho-pneumonia virus of rodents described by GONNERT.

Chemical and biological aspects of the chemotherapy of malaria are covered by 6 chapters in 56 pages. Chemical work in this field in Germany did not go far beyond exploration of quinoline and acridine derivatives, with "Sontochin" and "Endochin" among the quinolines as the best-known products. "Sontochin" was first tested in a limited way already as far back as 1937, and the story has often been told (though not in the volume under review) how a stock of this substance, of unknown composition at the time, was captured in North Africa in 1943, and then carefully studied in the U.S.A., where a closely similar compound, "Chloroquine" (which is "Sontochin" minus its 3-methyl group) eventually emerged as the most highly recommended product of the U.S. war-time drive for new antimalarial agents. "Endochin", among the quinolines, is an interesting departure from the classical heterocyclic alkylaminoalkylamine type of synthetic antimalarial. It is said to have given better results than paludrine in sporozoite infections of *P. cathemerium*, though not in those of *P. gallinaceum*, but it proved to be of little or no value in human malaria.

Other chapters deal with quaternary quinoline compounds as agents against trypanosomiasis and babesiasis; 4-aminoquinolines (such as Surfen C for *T. congolense* and 7602 Ac for *T. cruzi* infections); organic bases as amoebicides; metals and metalloids in general; sulphonamides and related compounds as both antimalarial and antibacterial agents; and the xanthone drugs (the "Miracils") for bilharziasis. Interesting short chapters deal with nitrobenzoic acid esters and isomers of N-methyl acridone as antibacterial substances, and with the curious discovery that replacement of the *p* : *p'* chlorine atoms of DDT by NO_2 groups converts this substance from an insecticide into a chemotherapeutic agent for experimental typhus infection.

Probably the most important German chemotherapeutic discovery during the war years was that of "Marfanil", a most opportune drug to have been produced in a time of war on account of its great superiority over sulphonamides in the presence of pus and as an agent against gas gangrene. It would no doubt have been generally acclaimed as an outstanding discovery had it not been completely outclassed by the development of penicillin in Britain and America. Antibiotics received scant attention in Germany during the war.

There are many interesting points of detail which it would be tempting to quote, but space can now permit of only a few general comparisons, which this volume prompts, between war-time work on chemotherapy in Germany on the one hand and in Britain and the U.S.A. on the other.

There seem to have been no fundamental contributions to the study of modes of drug action in Germany during the war. No doubt the spirit of the times and of the leaders forbade such seemingly idle preoccupations. By contrast, it is indeed remarkable that purely theoretical studies on chemotherapy should have enjoyed a swift impetus in Britain and the United States during the war years. The work of FILDES and his school stimulated what is almost a new science in the study of so-called "metabolite antagonists" (based though it is on long-established concepts in enzymology). So fertile has this development been that it was possible for ROBLIN in 1946 to publish a review on the subject (*Chem. Reviews*, v. 38, 255), embodying 471 literature-references, 417 of which date since 1939. It is surely not an unrelated fact that Britain and the United States should none the less have outstripped Germany also in results of "practical" value during the war.

With regard to malaria, there appear to have been no far-reaching or novel studies on the life-cycle of the parasite, so fundamentally significant for successful chemotherapy of this infection. The Germans continued to depend on the ROEHL test in canaries for schizonticidal activity, supplemented by the use of rice-finches for gametocidal effects. The resourceful utilization of chicks and, to a less extent, of ducklings in Britain and the U.S.A., breaking entirely new ground in methods of large-scale routine assay for possible antimalarials, saw no counterpart in Germany. It is striking how the situation in regard to synthetic antimalarial remedies before and during the Second World War in one respect repeated the history of antisyphilitic remedies during the First World War. In both instances we were almost entirely dependent on Germany for these substances when the storm broke, and tremendous effort had then to be applied towards remedying the situation, from the very foundations upwards, while the war was actually being waged. Both the peril and the effort were indeed prodigious in regard to malaria during the recent war.

The volume under review gives very little information on chemotherapeutic investigations in man. It is understandable that there should be no mention of the malaria experiments on internees of Dachau, for which the distinguished investigator Claus SCHILLING was eventually convicted and executed, and there is food for moralist thought in the lack of tangible result from such use of human material, compared with the solid outcome of, for example, the rigorous investigations on volunteers by FAIRLEY in Northern Australia during the same period.

E. M. Lourie

GOARNISSON, J. **Guide médical africain.** [African Medical Handbook.] Préface du Docteur L. AUJOULAT. pp. xv+572, 99 figs. & 44 pls. (3 coloured). 1948. Issy-Les-Moulineaux: Les Presses Missionnaires, Editions Saint-Paul, 184 avenue de Verdun.

The author of this book is a medical missionary of the Society of African Missions (White Fathers) in the French territory of Upper Volta in West

Africa. Dr. Goarnisson began to teach African hospital assistants in 1931—first the diagnosis and treatment of sleeping sickness, and later general medicine and surgery. The book is intended primarily for his former pupils now engaged in medical work on their own, but he also envisages its use by missionaries, managers of industrial concerns, heads of families in remote places and finally medical practitioners. It is therefore difficult to know on which level to review it.

In the introduction the author informs the reader that the book does not contain all diseases and that he has deliberately left out those which are rare, or exceptional in the tropics. He would have done well to leave out a great deal more, for he gives so many treatments new and old that an inexperienced person seeking advice from the book on the treatment for example of pneumonia might wonder which of the six external and five internal methods of treatment given he should follow. The former include dry and wet cupping, and the latter fixation abscess and antipneumococcal serum, " which may replace the sulphonamides and fixation abscess but is less effective."

A well-illustrated outline of anatomy and physiology is followed by chapters on minor medical and surgical techniques. Some of these read like extracts from the catalogue of a museum of medical history but that they are by no means museum pieces to the author is shown by his inclusion of the fixation abscess already mentioned as a treatment which may be indicated in pneumonia, influenza, puerperal fever and cerebrospinal meningitis. Wet and dry cupping may be indicated in pulmonary infections, basal congestion due to cardiac failure, hepatic and renal congestion and lumbago.

In the treatment of cerebrospinal meningitis the first remedy mentioned is meningococcal serum, and the second the sulphonamides—septoplix, lysococcine, bacteramide and Dagénan. The first three of these are unfamiliar in British medical practice. In the treatment of lobar pneumonia, fixation abscess is mentioned along with sulphapyridine, to be used when the latter is contra-indicated and in serious cases. There is no mention of penicillin here although the penultimate chapter of the book gives an account of it.

The chapters on emergencies such as burns, haemorrhage, asphyxia and poisoning are good, as is that on bandaging, which is well and fully illustrated.

The dysenteries and helminthic infestations are well described.

In the account of pulmonary tuberculosis there is the extraordinary statement that transplacental infection is rarely due to the acid-fast bacillus but rather to the "tuberculous ultra-virus" which causes a benign and rarely fatal infection.

Simple catarrhal jaundice is said to be due to intestinal microbes which ascend the biliary passages without causing any severe lesion of the hepatic cells. [This is a very outmoded pathology.]

The diseases usually classed as tropical are well described. A full account of malaria is given and all the antimalarial drugs in common use are mentioned. Quinine is still given pride of place, and mepacrine is advised only when quinine is badly tolerated. Resochin is preferred to mepacrine, and paludrine is said to be less efficacious than the foregoing drugs, being active against *P. falciparum*, less active against *P. vivax*, and inactive against *P. malariae*. The only suppressants mentioned are quinine and mepacrine. Nothing new is said about blackwater fever.

The pains of dengue are said to be abolished immediately by lumbar puncture and the withdrawal of cerebrospinal fluid.

The chapter on trypanosomiasis is probably the best in the book. It includes an account of *T. gambiense* and of the five species of *Glossina* prevalent in the area. Mass examination of a population is described, and not only is there an account of the usual trypanocidal drugs but the official courses of treatment

laid down by the Government trypanosomiasis service are given in tables. Atoxyl and pentamidine are used in early cases and Orsanine and Tryparsamide in late cases. It should be noted that most of the information in this chapter is only applicable to the infection caused by *T. gambiense*.

A chapter on ophthalmology includes among many other things a detailed account of an operation for trichiasis. This may suggest that hospital assistants in the Upper Volta are accustomed to perform this operation on their own. A number of coloured drawings of common eye lesions are given. The laboratory section is too short, but contains an amount of practical information useful to hospital assistants, including diagrams of parasites and bacteria.

A White Sister has contributed an informative section on the care of babies, and this is of special value, for only too rarely have African hospital assistants any knowledge at all of the care of the young.

Dr. Goarnisson has evidently a vast experience of medical work in West Africa and his book would be of value to a teacher of African hospital assistants or dispensers or dressers in any part of tropical Africa, but it is doubtful whether it is of great value to the hospital assistants themselves in its present state. A severe pruning would, however, render it eminently useful.

H. G. Calwell

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